

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

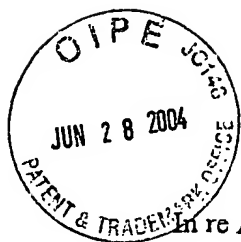
Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

: Attorney Docket No. DVME-1014USCON1

5 BOUCHER, CHARLES

Serial No. 10/058,622

: Group Art Unit: 1631

10 Filed: January 28, 2002

: Examiner: CHANNING MAHATAN

For: METHOD FOR EFFECTING COMPUTER IMPLEMENTED DECISION-SUPPORT IN  
THE SELECTION OF THE DRUG THERAPY OF PATIENTS HAVING A VIRAL DISEASE

DECLARATION OF CHARLES BOUCHER PURSUANT TO 37 C.F.R. §1.132

15 Assistant Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

20 Sir:

1. I, Charles Boucher, hereby declare as follows:

25 2. I am the sole inventor for the above-identified application.. My detailed *curriculum vitae* is attached hereto as Exhibit A.

30 3. I have reviewed the specification, drawings and currently pending claims of U.S. patent application no. 10/058,622. I have also reviewed the Office Action mailed on July 29, 2003 (hereinafter "the Office Action"), the applicant's response to the Office Action, which arrived at the United States Patent and Trademark Office (hereinafter "USPTO") on November 28, 2003, the Final Rejection mailed on February 24, 2004 (hereinafter "the Final Rejection"), the applicant's response to the Final Rejection, which arrived at the USPTO on April 26, 2004, and the Advisory Action mailed on May 12, 2004 (hereinafter "the Advisory Action").

35 4. I am informed that claims 21-63 of the present application stand rejected under 35 U.S.C. §112, 1<sup>st</sup> paragraph, as failing to comply with the enablement requirement.

5. I am informed that the standard for determining whether the specification meets the enablement requirement was set forth in *Mineral Separation v. Hyde*, 242 U.S.261,270 (1916), which posed the question, "is the experimentation needed to practice the invention undue or unreasonable?"

6. I am also informed that the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

*In re Wands*, 858 F.2d 731,737,8 USPQ2d 1400, 1404 (Fed.Cir.1988) and MPEP §2164.01(a).

**Claim 21**

7. With regard to the breadth of claim 21, claim 21 of the present application is relatively narrow since it requires the use of a rules database wherein each rule indicates the suitability of a drug for treatment of a specific viral genotype. Moreover, the method of claim 21 displays drugs suitable for therapy in a ranking based on their suitability indication. The suitability indication is based on at least a combination of: (a) a first value indicating resistance level of the genotype for that drug, and (b) a second value indicating the confidence in the first value. Thus, to perform the method of independent

claim 21, a skilled person must be able to provide a rules database that gives a suitability indication, based on the first and second values (a)-(b).

8. With regard to the nature of the invention, the invention relates to a method for computer implemented decision support in selection of drug therapy. As such, the invention lies in an improved computer implementation of a specific type of mental process that doctors carry out on a regular basis, albeit without computer implementation. More particularly, doctors currently make selections of appropriate drug therapies. Such selections are often based on factors such as the resistance level of a particular genotype for a particular drug, as well as the degree of confidence the doctor has in the information that is relied upon for determining the resistance level of that genotype for that drug. Therefore, the nature of the invention is such that the skilled person already knows how to select a drug therapy, by the performance of a mental process, using the type of information required by claim 1 of the present application.
9. The state of the prior art is evidenced by, for example, two of the documents of record in the present application, namely, "CTSHIV: A Knowledge-Based System for the Management of HIV-infected Patients," Pazzani et al., *Proceedings: Intelligent Information Systems, IIS' 97* (CAT. No. 97TB100201), 1997, pages 7-13 (hereinafter "Pazzani et al."); and "Knowledge-Based Avoidance of Drug-Resistant HIV Mutants," Lathrop et al., *American Association of Artificial Intelligence*, 1998, pages 1071-1078 (hereinafter "Lathrop '98"). Lathrop '98 describes the CTSHIV system that is employed in the method of Pazzani et al.
10. The level of ordinary skill in the art is high. Specifically, Lathrop '98 describes an AI system (CTSHIV) that connects the scientific literature describing specific HIV drug resistances directly to the customised treatment strategy of a specific HIV patient. Rules in the CTSHIV knowledge base encode knowledge about sequence mutations in the HIV genome that have been found to result in drug resistance to the HIV virus. The rules represent knowledge about HIV drug resistance as a set of if-then rules of the form:

IF <antecedent> THEN <consequent> [weight]

5 The system described in Pazzani et al. uses the CTSHIV expert system that is described in Lathrop '98. Thus, from Pazzani et al. and Lathrop '98, it is clear that the skilled person already knows how to implement a rules database wherein a suitability indication is based on a value indicating resistance level of the genotype for that drug, i.e. element (a) of claim 1 of the present application.

10 11. Lathrop '98 also teaches that, "The weight associated with a rule is not a confidence as in many expert systems. Rather it reflects the estimated level of resistance to a particular drug." (See page 1073, last paragraph of Lathrop '98). This statement indicates that, as of 1998, there were many expert systems in existence, which employed a confidence value to determine the weight associated with a particular rule  
15 in a knowledge-based system. In my opinion, this demonstrates that, as of 1998, a skilled person was capable of implementing element (b) of claim 1 of the present application, namely, basing a suitability indication on a value indicating the confidence in the value indicating a resistance level of the genotype for that drug.

20 12. The level of predictability in the art of computer-implemented decision support is very high since this art involves the application of a rules database, using a computer. Thus, a skilled person can predict, from knowledge of the rules database, what the outcome of the method will be. The skilled person can also predict the effect of a change in the rules database on the outcome of the method, from knowledge of the rules database.

25 13. A very significant amount of direction is provided in the present application for implementation of the method of claim 1. For example, the specification discusses how the conferred resistance by substitution is derived and how a value is assigned  
30 indicative of resistance level. See page 3, line 31, to page 5, line 11, of the application as originally filed. This part of the application explains, among other things, that the information on the conferred resistance by substitutions is obtained from scientific articles and evaluations by pharmaceutical companies, which information is carefully

examined by the experts of a core-committee. In the end the core-committee assigns a value indicating the resistance level. See page 4, lines 15-18 of the application as originally filed. In my opinion, the direction given in the application on how to assign a value indicating the resistance level, is sufficient for a person skilled in the art to implement this aspect of the claimed invention since, as discussed above with respect to the state of the art, the skilled person already knows, from Pazzani et al. and Lathrop '98, how to create a rules database which assigns a value indicating resistance level.

14. Also, the specification at page 5, line 35, to page 6, line 6, sets forth an example of how to determine the confidence level. In this example, objective criteria are employed. Specifically, the confidence level may be one of three levels, namely, (1) the drug result is based on suggestive evidence, (2) the drug result is proven *in vitro*, or (3) the drug result is proven *in vivo*. In my opinion, it is straightforward for a person of ordinary skill in the art to assign a confidence level on this basis since that person need only read the experimental portion of the information in question to determine whether tests were carried out *in vivo*, *in vitro*, or otherwise. Moreover, the skilled person is already familiar with expert systems employing confidence levels as weighting factors, as discussed above with respect to Lathrop '98, and thus would have no difficulty in implementing the present method based on the application of common general knowledge and the detailed teaching of how to assign a confidence level that is provided in the present specification at page 5, line 35 to page 6, line 6.

15. In addition, the specification of the present application describes how to assign the suitability level at page 6, lines 8-26. This description is sufficient for a skilled person because the suitability level is the resistance level weighted based on a confidence value. As discussed above, Lathrop '98 makes it clear that many expert systems already existed as of 1998 wherein a first value is weighted based on a second confidence value.

16. Furthermore, the present specification extensively describes the manner of updating the rules database on page 3, line 31, to page 4, line 18, of the application as originally filed. Specifically, the rules database is updated by a core committee that periodically

reviews, on a frequent basis, the latest publications on the subject and decides which adjustments should be made to the rules, based on these latest publications.

17. The present specification contains an extensive working example at pages 7-12 and in Figures 1-3 of the present specification.

18. In my opinion, essentially no experimentation is required to implement the present invention based on the disclosure of the application as filed, taken in combination with the common general knowledge of a skilled person. As discussed above, the skilled person already knows how to assign a first resistance value from Pazzani et al. and Lathrop '98, the specification provides an objective method of determining a confidence value that can easily be carried out by a skilled person, and the skilled person already knows how to weight a first value based on a confidence value, as can be concluded from Lathrop '98 which teaches that many such expert systems were already in existence in 1998.

#### Claim 44

19. The method of claim 44 can be carried out by a skilled person in the same manner as discussed above with respect to claim 21, except that in the method of claim 44, the rules database must include a rule for determining the suitability of a drug for treatment of a specific viral genotype, when that drug is taken in combination with another drug.

20. In my opinion, the skilled person can implement the method of claim 44 with essentially no experimentation since the skilled person can easily implement the only further step required by claim 44, that is not present in the method of claim 21. For example, the skilled person can formulate a rule for determining the suitability of a drug for treatment of a specific viral genotype, when that drug is taken in combination with another drug in the same manner that the first value indicating resistance level is formulated in the method of claim 21, except that in this case the skilled person would refer to information relating to particular combinations of drugs to formulate the resistance value, rather than to information relating to the use of individual drugs. Thus, the skilled person would have no difficulty in implementing the method of claim

44 of the present application in view of the disclosure of the present specification and the common general knowledge of a person skilled in the art.

**Claim 51**

5        21.     The method of claim 51 can be carried out by a skilled person in the same manner as discussed above with respect to claim 21, except that in the method of claim 51, the rules database must include a rule for determining the suitability of a drug for treatment of a specific viral genotype which takes into account the level of the drug in a patient.

10       22.     In my opinion, the skilled person can implement the method of claim 51 with essentially no experimentation by including as a data input to the rules database, the level of the drug in the patient, as specified in the information relied upon for creation of the rules database. Then, when a suitability indication is desired, the skilled person may specify or determine the desired drug level so that the rules database will limit its  
15       consideration of information to only information relevant to the specified drug level. This will generate a list of drug therapies, which are based on a resistance value at a particular drug level, as required by the method of claim 51.

**Claim 60**

20       23.     The method of claim 60 can be carried out by a skilled person in the same manner as discussed above with respect to claim 21, except that in the method of claim 60, the rules database must include a rule for determining the suitability of a drug for treatment of a specific viral genotype which takes into account the clade of a virus.

25       24.     In my opinion, the skilled person can implement the method of claim 60 with essentially no experimentation by including as a data input to the rules database, the clade of the virus, as specified in the information relied upon for creation of the rules database. Then, when a suitability indication is desired, the skilled person may specify or determine the clade so that the rules database will limit its consideration of  
30       information to only information relevant to the specified clade. This will generate a list of drug therapies, which are based on a resistance value for a particular virus clade, as required by the method of claim 60.



**Dependent Claims**

25. Some of the dependent claims of the present application require rules for different protein substitutions and/or type of drug activity. In my opinion, the skilled person can implement the methods of these dependent claims with essentially no experimentation by including as a data input to the rules database, the protein substitutions and/or type of drug activity, as specified in the information relied upon for creation of the rules database. Then, when a suitability indication is desired, the skilled person may specify the protein substitutions and/or type of drug activity so that the rules database will limit its consideration of information to only information relevant to the specified protein substitutions and/or type of drug activity. This will generate a list of drug therapies, which are based on a resistance value for a particular protein substitution and/or type of drug activity, as is required by these dependent claims.

26. Some of the dependent claims of the present application require consideration of clinical experience in determining a suitability indication. According to the specification at page 6, lines 27-31, clinical experience can mean experience provided by experts, or it can comprise the outcome of clinical studies relating the presence of substitutions at the start of therapy directly to clinical or virological outcome. In my opinion, substantially no experimentation is required to consider clinical evidence in determining a suitability indication. For example, in the case of experience provided by experts, the experts can simply weight the suitability indication based on their own clinical experience, e.g. an expert that has a significant amount of favorable clinical experience will raise the suitability indication to reflect the favorable clinical experience. In the case of using the outcome of clinical studies as the clinical experience, the incorporation of this information can be done in essentially the same way that the information relating to the resistance level is incorporated into the rules database.

27. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that the statements were made with the knowledge that willful false statements and the like

made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

5

Respectfully submitted,

By:

Charles Boucher

10

Dated:

June 18,  
2004

## **CURRICULUM VITAE**

Name Charles Achim Bernard Boucher, MD, PhD  
Place of birth Amsterdam  
Date of birth January 16, 1958  
Nationality Dutch and Belgian  
Home address Kromme Nieuwegracht 21, 3512 HD Utrecht, the Netherlands  
telephone home (31-30) 234 20 10, mobile 31651203640

### **Education**

1970-1977 Barlaeus Gymnasium, Amsterdam  
1977 Gymnasium Beta  
1977-1983 Study Medicine, University of Amsterdam, Faculty of Medicine  
1983 Doctoraal degree  
1983-1987 Medical internships  
1986 Visiting fellow, School of Medicine, Yale University, USA  
1987 Cum Laude Medical degree (MD)  
1987-1991 Medical microbiologist training  
Academic Medical Centre, University of Amsterdam  
1991 Board certification clinical microbiologist  
1993 Ph.D.-degree University of Amsterdam, Faculty of Medicine .  
Thesis: "Characterisation of human immunodeficiency viruses during zidovudine treatment"

### **Present position and Assignments**

Associate Professor in Virology, Department of Virology, Eijkman Winkler Institute, Faculty of Medicine, University Medical Center Utrecht.

Coordinator of a grant from the European Commission to form a network of 16 European countries entitled Spread, A Network to control spread of HIV drug resistance.

Scientific Advisor Virology Education BV Utrecht.

Visiting Associate Professor, University of Stanford, School of Medicine, Stanford, CA, USA

## Professional and scientific experience

- 1983-1985 Research assistant clinical virology Department of Medical Microbiology, University of Amsterdam head: Prof. Dr J. van der Noordaa.
- 1989 Scholarship on behalf of the Royal Dutch Academy of Sciences.  
Visiting fellow, Department of Paediatrics, Division of Infectious Disease. Yale University, New Haven, Connecticut, USA, head: Prof. G Miller.
- 1987-1991 Specialisation in clinical microbiology, Medical Microbiology Department, Academic Medical Centre, head Prof. Dr J. van der Noordaa
- 1989-1993 Doctoral research: Virological effects of zidovudine treatment  
Medical Microbiology Department.. Human Retrovirus Laboratory, head Prof. Dr J. Goudsmit, Academic Medical Centre, University of Amsterdam
- 1989 Visiting fellow, Wellcome Research Laboratories, Molecular Sciences Department, Beckenham, England Research: "Detection of zidovudine resistance causing mutations" head Dr G. Darby
- 1991-1995 Head of the Antiviral Therapy Laboratory, Medical Microbiology Department, Academic Medical Centre, head Prof. Dr J. van der Noordaa.
- 1995- Associate professor in clinical Virology, Department of Virology, Eijkman-Winkler Institute for Medical Microbiology, University Medical Centre Utrecht, head Prof. Dr. J. Verhoef.
- 1997-2001 Co-ordinator Grant from the European Commission. European Network for Evaluation of AIDS therapy ENVA'
- 2001- Visiting associate professor, School of Medicine, Stanford University

## Education and teaching

- 1987-89 Inleiding medische microbiologie voor OK verpleegkundigen
- 1987-91 Training coassistenten geneeskunde in handvaardigheden en interpretatie van medisch microbiologische technieken
- 1992 Docent voor tweede studiejaar geneeskunde klinisch lijnonderwijs
- 1994 Diagnostiek en therapie van infecties, cursus voor assistenten interne geneeskunde en microbiologie, 17 december 1992. Antiretrovirale therapie
- 1993 Docent voor derde studiejaar geneeskunde klinisch lijnonderwijs
- 1993 Hoofdvakbegeleider vierde jaars student medische microbiologie
- 1993 Nascholingscursus HIV Infectie & AIDS. HIV: biologisch fenotype en resistentie. Stichting Nascholingscursus inwendige geneeskunde Amsterdam (NIGA), Heelsum, 4-5 maart.
- 1996 7th Utrecht Medical Summer School, 8-25 July, 1996: Principles and Practice of Infectious Diseases "Therapy of HIV infection; new insights"
- 1996-2003 Verzorging cyclus Virologie derde studiejaar geneeskunde.
- 1997 Vakgroep Immunologie Caput College "Therapy of HIV anno 1997."
- 1997 Gastcollege Rega Instituut, Katholieke Universiteit Leuven, België  
*Anti-HIV therapy and resistance, in vitro and in vivo evaluation.*
- 1997 Voordracht t.b.v. Catharijneg cursus, Universiteit Utrecht  
*Techniek en toepassingsmogelijkheden van PCR*
- 1997 Deelname aan collegeprogramma Speciele Farmacologie/Psychofarmacologie, 4e jaars studenten geneeskunde, 1e semester '97/'98. Rudolf Magnus Instituut voor Neurowetenschappen. Universiteit van Utrecht. *Virustatica*
- 1999 Lid nieuwe curriculum commissie geneeskunde, Faculteit Geneeskunde Universiteit Utrecht.
- 1996 Co-promotor bij de promotie van M.D. de Jong, proefschrift *Drug-failure in HIV-1 infection causes and implications for therapeutic strategies*, Universiteit van Amsterdam
- 1997 Lid van Promotiecommissie bij de promotie mw. drs. A.B. van 't Wout op 18 juni 1997, Universiteit van Amsterdam.
- 1997 Lid van Promotiecommissie bij de promotie Dr. A.A. Imrie *Genotypic and phenotypic characterization of transmitted human immunodeficiency virus type-1*. University of New South Wales, Australia
- 1998 Lid van Promotiecommissie bij de promotie Dr B. B. Oude Essink *Reverse transcription of the HIV-1 genome*. Universiteit van Amsterdam

- 1998 Co-promotor bij de promotie van Dr. A.M. Been-Tiktak *Clinical and Virological Evaluation of Ateviridine and Delavirdine. Nucleoside Reverse Transcriptase Inhibitors*. Universiteit van Utrecht
- 1999 Co-promotor bij de promotie van Dr. M Nijhuis. *Fitness of HIV-1 during antiretroviral therapy*. Universiteit van Utrecht.
- 1999 Lid van Promotiecommissie bij de promotie van Dr. D. W. Notermans. *The 'triple study' Viral dynamics and immune reconstruction in HIV-1 infection during potent antiretroviral therapy*. Universiteit van Amsterdam.
- 2000 Co-promotor bij de promotie van Dr. W Keulen. *Evolution of drug-resistant HIV-1 variants*. Universiteit van Utrecht
- 2001 Lid van Promotiecommissie bij de promotie van Dr. M. E. van Praag, . *Anatomical and cellular reservoirs for HIV during potent antiretroviral therapy*, Universiteit van Amsterdam
- 2001 Lid van examencommissie bij de promotie van Dr. K Van Vaerenbergh . *Study of the impact of HIV genotypic drug resistance testing on therapy efficacy*. Universiteit van Leuven
- 2001 Co-promotor bij de promotie van Dr. J.C. Stuart, *HIV and the immune system during highly active antiretroviral therapy*. Universiteit van Utrecht
- 2003 Lid van Promotiecommissie bij de promotie van Dr. C. Da Fonseca Pereira . *HIV-1 neuropathogenesis and antiviral research*. Universiteit van Utrecht
- 2003 Lid van de organizing committee "Course epidemiological principles of infectious diseases". April 22 – 25, 2003
- 2003 Lid van de Promotiecommissie bij de promotie van Dr. M.G.J. van Kraaij. Promotie op 7 Oktober 2003.

## Organisational Activities

- Initiator and member of the Organising committee of the Annual International Workshop on HIV-Drug Resistance.
  - 1992 Noordwijk, the Netherlands
  - 1993 Noordwijk, the Netherlands
  - 1994 Kuai, Hawaii, USA
  - 1995 Sardinia, Italy
  - 1996 Whistler, Canada
  - 1997 St. Petersburg, USA
  - 1998 Baveno / Lake Maggiore, Italy
  - 1999 San Diego, USA
  - 2000 Barcelona Spain
  - 2001 Scotsdale USA
  - 2002 Sitges Spain
  - 2003 Cabo Mexico
- Initiator and member of the Organising committee of the Annual International workshop on HIV Pharmacology
  - 2000 Noordwijk the Netherlands
  - 2001 Noordwijk the Netherlands
  - 2002 Washington, USA
  - 2003 Cannes France
- Organiser of the Dynamics of HIV Infection Meeting 1995 Arden Conference Centre, Harriman, New York, USA.
- International Editor of 'Timely Topics in Medicine SIDA', <http://www.prous.com/ttmsida>; the AIDS Cyber Journal.
- Guest-editor Antiviral Therapy
- Co-chair International Consensus Symposium on Combined Antiviral Therapy and Implications for Future Therapies.
  - 1995 Lisbon, Portugal
  - 1996 Barcelona, Spain
- Session-chair at NHG Referatendag 12.5.1998.
- Joint-Reviewer of '2nd International Workshop on HIV Drug Resistance and Treatment Strategies' *International Antiviral News* July 1998, 6(7): 130-139.
- Chairman of free lectures at the Microsymposium "Opportunisme in de infectieziekten", 47ste Wetenschappelijke Vergadering VIZ, Utrecht, October 16, 1998
- Chairman 4th International Congress on Drug Therapy in HIV Infection; plenary session 3: Virology, Resistance and Clinical Implications, Glasgow, UK, 8-12 november 1998.
- Interview Radio 1 op 12 augustus 1997. *De aidscocktail leek zo veelbelovend.*
- Coordinator van de discussie over HIV/AIDS: *Is HIV-eradication possible and will it lead to a complete recuperation of the immune system in the treated patient?* Gehouden op het AIO Seminar Course Infection & Immunity, 12-15 Januari 1998 te Utrecht.

- Roche mini-Symposium 'Aidszorg in de praktijk'. West-Indische Huis, Amsterdam, January 23, 1998. ( C.A. Boucher *Virologie*)
- Workshop chairman during the IXth International Conference on AIDS, Berlin 7-11 juni 1993.
- Workshop chairman during the 4 Muncher AIDS Tage 1994. Satellitensymposium II Resistenz gegen antiretrovirale substanzen: Grundlagen, Erkennung, Klinische Konsequenzen.
- Co-chair 6th Annual International Discussion Meeting on HIV Dynamics and Evolution, Atlanta, Georgia, USA, March 26-29, 1999. Session: Dynamics and evolution of HIV antiviral resistance.
- Chairman of the II International Workshop on HIV eradication, Fundacio irsiCaixa (1999)
- Chairman of the First International Symposium on Diagnostic Technologies for HIV/AIDS and Other Life-Threatening Illnesses (1999)
- Member of the 'Comitato Scientifico' of ReAd Files, Italy. January 2000
- Chair during the NAM symposium on "Emerging Therapies for HIV Infection: new targets and sustainable strategies" in London on May 9th 2003.
- Panelmember during the session "Clinical Cases" as part of the 9th European AIDS Conference (EACS) in Warsaw, Poland. Date: October 28, 2003.
- Co-chair of the 4rd International Workshop on HIV Eradiction held on November 14th 2003 in Barcelona.
- Chair during the 1st International Workshop on HIV Persistence during Therapy held from December 10 – 12, 2003 in St. Martin. December 11th, Session IV: Primary HIV Infection, Transmission & Eradication Issues.
- Chair during the Interactive Resistance Workshop in Berlin held on March 8th 2004.
- Interview bij AVRO's 1 op de middag op over *de Vogelgriep* 2 februari 2004.
- OC member of the 5th International Workshop on Clinical Pharmacology of HIV Therapy held in Rome from April 1st until April 3rd 2004.

1990-91	Lid van bestuur Vereniging voor arts-assistenten medische microbiologie
1992-94	Lid van het dagelijks bestuur van de vakgroep medische microbiologie
1993-94	Adviserend lid Faculteitsraad Geneeskunde Universiteit van Amsterdam.
1994-95	Gekozen lid faculteitsraad Geneeskunde, Universiteit van Amsterdam.

Scientific consultant for:

Wellcome Reseach Laboratories UK/ Glaxo Group Research UK,  
Janssen Pharmaceuticals Belgium,



Hoechst AG Germany, Upjohn USA,  
Roche Medical Systems Alameda USA  
Roche Pharmaceuticals, Swiss  
Bristol-Myers Squibb, USA  
Boehringer Ingelheim  
Abbott Diagnostics

Scientific reviewer for:

Journal of Infectious Disease  
Lancet  
Acta Clinica Belgica  
AIDS  
Antiviral Research  
Antimicrobial Agents and Chemotherapy  
Journal of Virology  
Proceedings National Academy of Sciences  
Journal of AIDS

## **Memberships**

Advisory Board Paediatric Network on Treatment of Children with AIDS,  
European Community.

Advisory Board European Collaborative Study on HIV transmission, European  
Community

Antiviral Research Society.

American Society for Microbiology.

American Academy of Science.

New York Academy of Sciences.

Editorial board of "Antiviral Therapy".

European Group of Rapid Viral Diagnosis.

International AIDS Society.

Dutch AIDS Treating Physician's Society.

Commission Genetic Modification of the Ministry of Housing, Spatial Planning  
and Environment.

European Society for Paediatric Infectious Diseases.

Editorial Board member of ReAd files, Project for a newsletter on HIV drug  
resistance & adherence to antiretroviral therapy.

Member of the Editorial Board of Current Opinion in Anti-infective Investigational  
Drugs.

International Association of Physician in AIDS Care (IAPAC).

Editorial Board of Antimicrobial Agents and Chemotherapy.

Scientific Advisory Committee for the Collaborative Research Seminar on HIV Entry and Fusion Inhibition, December 2000

Editorial board HIV resistance.web.

Editorial board HIVpharmacology.com.

Member of the "Platform HIV/AIDS Onderzoek en Behandeling in ontwikkelingslanden".

## I Peer reviewed publications

1. Boucher, C.A.B., Gans de, J., Oers van, R., Danner, S.A. and Goudsmit, J. Transmission of HIV and AIDS by plasmapheresis for Guillain-Barré Syndrome. *Clin.Neurol.Neurosurg.* (1988) 90,3:235-36.
2. Epstein, L.G., Boucher, C.A.B., Morrison, S.H., Connor, E.M., Oleske, J.M., Lange, J.M.A., Noordaa van der, J., Bakker, M., Dekker, J.T., Scherpblor, H., Berg van den, H., Boer, K. and Goudsmit, J. Persistent human immunodeficiency virus type 1 antigenemia in children correlates with disease progression. *Pediatrics* (1988) 82,6:919-24.
3. Goudsmit, J., Boucher, C.A.B., Meloen, R.H., Epstein, L.G., Smit, L., Hoek van der, L. and Bakker, M. Human antibody response to a strain-specific HIV-1 gp120 epitope associated with cell fusion inhibition. *AIDS* (1988) 2:157-164.
4. Pronk, J.C., Frants, R.R., Crusius, B., Eriksson, A.W., Wolf de, F., Boucher, C.A.B., Bakker, M. and Goudsmit, J. No predictive value of GC phenotypes for HIV infection and progression to AIDS. *Hum.Genet.* (1988) 80:181-182.
5. Reiss, P., Lange, J.M.A., Boucher, C.A.B., Danner, S.A. and Goudsmit, J. Resumption of HIV antigen production during continuous zidovudine treatment. *The Lancet* (1988) i:421.
6. De Wit, R., Boucher, C.A.B., Veenhof, K.H.N., Schattenkerk, J.K.M.E., Bakker, P.J.M., and Danner, S.A. Clinical and virological effects of high-dose recombinant interferon-alpha in disseminated AIDS-related kaposi's sarcoma. *The Lancet* (1988) 2:1214-17.
7. Boucher, C.A.B., Wolf de, F., Houweling, J.T.M., Bakker, M., Dekker, J., Roos, M.T.L., Coutinho, R.A., Noordaa van der, J. and Goudsmit, J. Antibody response to a synthetic peptide covering a LAV-1/HTLVIIIB neutralization epitope and disease progression. *AIDS* (1989) 3:71-76.
8. Boucher, C.A.B., Jager de, M.H., Debouck, C., Epstein, L.G., Wolf de, F., Wolfs, T.F.W. and Goudsmit, J. Antibody response to human immunodeficiency virus type 1 protease according to risk group and disease stage. *Journal of Clinical Microbiology* (1989) 7,7:1577-1581.
9. Goudsmit, J., Dekker, J.T., Boucher, C.A.B., Smit, L., Ronde de, A., Debouck, C. and Barin, F. Serum reactivity to HIV-1 accessory gene products distinguishes East African from West African HIV strains as infecting agent. *AIDS Res.Human.Retrov.* (1989) 5,5:457-77.
10. Lelie, P.N., Poel van der, C.L., Reesink, H.W., Huisman, J.G., Boucher, C.A.B. and Goudsmit, J. Efficacy of the latest generation of antibody assays for (early) detection of HIV 1 and HIV 2 infection. *Vox Sang.* (1989) 56:59-61.
11. Tijn van, D.A., Boucher, C.A.B., Bakker, M. and Goudsmit, J. Antigenicity of linear B-cell epitopes in the C1, V1, and V3 region of HIV-1 gp120. *Journal of acquired immune deficiency syndrome* (1989) 2:303-06.
12. Boucher, C.A.B., Krone, W.J.A., Goudsmit, J., Meloen, R.H., Naylor, P.H., Goldstein, A.L., Sun, D.K. and Sarin, P.S. Immune response and epitope mapping of a candidate HIV-1 p17 vaccine HGP30. *J.Clin.Lab.Anal.* (1990) 4,1:43-47.
13. Boucher, C.A.B., Tersmette, M., Lange, J.M.A., Kellam, P., Goede de, R.E.Y., Mulder, J.W., Darby, G., Goudsmit, J. and Larder, B.A. Zidovudine sensitivity of human

- immunodeficiency viruses from high-risk, symptom-free individuals during therapy. *The Lancet* (1990) 336:585-590.
14. Lange, J.M.A., Boucher, C.A.B., Hollak, C.E.M., Wiltink, E.H.H., Reiss, P., Royen van, E.A., Roos, M., Danner, S.A. and Goudsmit, J. Failure of prophylactic zidovudine after accidental exposure to HIV-1. *New Engl.J.Med.* (1990) 322:1375-1377.
  15. Richel, D.J., Lepoutre, J.M.M., Kapsenberg, J.G., Ooms, E.C.M., Boom, R., Boucher, C.A.B. and Kluin, P.M. Epstein-Barr virus in a CD8-positive T-cell lymphoma. *Am.J.Pathol.*(1990) 136:1093-99.
  16. Reiss, P., Wolf de, F., Kuiken, C.L., Ronde de, A., Dekker, J., Boucher, C.A.B., Debouck, C., Lange, J.M.A. and Goudsmit, J. Contribution of antibody response to recombinant HIV-1 gene-encoded products nef, rev, tat, and protease in predicting development of AIDS in HIV-1 infected individuals. *Journal of acquired immune syndrome* (1991) 4,2:165-172.
  17. Wolfs, T.F.W., Jong de, J.-J., Boucher, C.A.B., Hartman, S., Schipper, P., Keulen, W., Nara, P. and Goudsmit, J. Naturally occurring mutations of the HIV-1 V3 domain at positions crucial for antibody binding also affect biological phenotype. *Virology* (1991) 185:195-205.
  18. Boucher, C.A.B., Lange, J.M.A., Miedema, F., Weverling, G.J., Koot, M., Mulder, J.W., Goudsmit, J., Kellam, P., Larder, B.A. and Tersmette, M. HIV-1 biological phenotype and the development of zidovudine resistance in relation to disease progression in asymptomatic individuals during treatment. *AIDS* (1992) 6:1259-64.
  19. Boucher, C.A.B. Clinical significance of zidovudine-resistant human immunodeficiency viruses. *Res.Virology* (1992) 143:134-36.
  20. Boucher, C.A.B. and Lange, J.M.A. HIV-1 sensitivity to zidovudine and clinical outcome. *The Lancet* (1992) 339:626.
  21. Boucher, C.A.B., O'Sullivan, E., Mulder, J.W. Ramautarsing, C., Kellam, P., Darby, G., Lange, J.M.A., Goudsmit, J. and Larder, B.A. Ordered appearance of zidovudine resistance mutations during treatment of 18 human immunodeficiency virus-positive subjects. *Journal of Infectious Diseases* (1992) 165:105-10.
  22. Kellam, P., Boucher, C.A.B. and Larder, B.A. Fifth mutation in HIV-1 reverse transcriptase contributes to the development of high level resistance to zidovudine. *Proc.Natl.Acad.Sci.USA* (1992) 89:1934-38.
  23. Björling, E., Boucher, C.A.B., Samuelsson, A., Wolfs, T., Utter, G., Norrby, E. and Chiodi, F. Two highly antigenic sites in the human immunodeficiency virus type 1 reverse transcriptase. *Journal of Clinical Microbiology* (1993) 31:588-92.
  24. Boucher, C.A.B., Leeuwen, R.van, Kellam, P., Schipper, P., Tijnagel, J., Lange, J.M.A. and Larder, B.A. Effects of discontinuation of zidovudine treatment on the zidovudine sensitivity of HIV-1 isolates. *Antimicrobial Agents and Chemotherapy*. (1993) 37:1525-30.
  25. Boucher, C.A.B., Cammack, N., Schipper, P., Schuurman, R., Rouse, P.L. and Cameron, J.M. High level resistance to (-) enantiomeric 2'-deoxy-3'-thiacytidine (3TC) in vitro is due to one amino acid substitution in the catalytic site of HIV-1 reverse transcriptase. *Antimicrobial Agents and Chemotherapy*. (1993) 37:2231-34.
  26. Gao, Q., Gu, Z., Parniak, M.A., Cameron, J., Cammack, N., Boucher, C.A.B. and

- Wainberg, M.A. The same mutation that encodes low-level human immunodeficiency virus type 1 resistance to 2',3'-dideoxyinosine and 2',3'-dideoxycytidine confers high-level resistance to the (-) enantiomer of 2',3'-dideoxy-3'-thiacytidine. *Antimicrobial Agents and Chemotherapy*. (1993) 37:1390-92.
27. Lange, J.M.A., Teeuwssen, V.J.P., Boucher, C.A.B., Vahlne, A., Barin, F., Tjong-A-Hung, S., Dekker, J., Parkhede, U., Wolf de, F. and Goudsmit, J. Antigenic variation of the dominant gp41 epitope in Africa. *AIDS* (1993) 7:461-67.
  28. Zwart, G., Wolfs, T.F.W., Bookelman, R., Hartman, S., Bakker, M., Boucher, C.A.B., Kuiken, C. and Goudsmit, J. Greater diversity of the HIV-1 V3 neutralization domain in Tanzania compared with The Netherlands. *AIDS* (1993) 7:467-74.
  29. Bruisten, S.M., Koppelman, M.H.G.M., Roos, M.T.L., Loeliger, A.E., Reiss, P., Boucher, C.A.B. and Huisman, H.G. Use of competitive polymerase chain reaction to determine HIV-1 levels in response to antiviral treatments. *AIDS* (1994) 7, suppl.2:S15-S20.
  30. Frissen P.H.J., Ende van der M.E., Ten Napel C.H.H., Weigel H.M., Schrey G.S., Kauffmann R.H., Koopmans P.P., Hoepelman A.I.M., Boer de J.B., Weverling G.J., Haverkamp G., Dowd P, Miedema F., Schuurman R, Boucher C.A.B., Lange J.M.A. Zidovudine and Interferon-Alpha combination therapy versus zidovudine monotherapy in subjects with symptomatic human immunodeficiency virus type 1 infection. *J. Infect Dis* (1994)169:1351-5.
  31. Jong de, M., Loewenthal, M., Boucher, C.A.B., Ende, I. van der, Hall, D., Schipper, P., Imrie, A., Weigel, H., Kauffmann, R.H., Koster, R., Seville, P., Rocklin, R., Cooper, D.A. and Lange, J.M.A. Alternating treatment with nevirapine and zidovudine of HIV-1 infected individuals does not prolong nevirapine therapy. *Journal of Infectious Diseases* (1994)169:1346-50.
  32. Kellam, P., Boucher, C.A.B., Tijnagel, J.M.G.H., and Larder, B.A. Zidovudine treatment results in the selection of human immunodeficiency virus type 1 variants whose genotypes confer increasing levels of drug resistance. *J.Gen. Virol.* (1994) 75:341-51.
  33. Boucher, C.A.B., Larder, B. HIV Variation: Consequences for antiviral therapy and disease progression. *Reviews in Medical Virology* (1995) 5:7-21.
  34. Danner, S.A., Carr, A., Leonard, J.M., Lehman, L.M., Gudiol, F., Gonzales, J., Raventos, A., Rubio, R., Bouza, E., Pintado, V., Aguado, A.G., Delomas, J.G., Delgado, R., Borleffs, J.C.C., Hsu, A., Valdes, J.M., Boucher, C.A.B., Cooper, D.A., Geimeno, C., Clotet, B., Tor, J., Ferrer, E., Martinez, P.L., Moreno, S., Zancada, G., Alcamí, J., Noriega, A.R., Pulido, F., and Glassmann, H.N. A short-term study of the safety, pharmacokinetics, and efficacy of ritonavir, an inhibitor of HIV-1 protease. *N Engl J Med* (1995) 333:1528-1533.
  35. Danner, S.A., Carr, A., Leonard, J.M., Lehman, L.M., Gudiol, F., Gonzales, J., Raventos, A., Rubio, R., Bouza, E., Pintado, V., Aguado, A.G., Delomas, J.G., Delgado, R., Borleffs, J.C.C., Hsu, A., Valdes, J.M., Boucher, C.A.B., Cooper, D.A. Safety, pharmacokinetics, and preliminary efficacy of ritanovir, hibitor of HIV-1 protease. *New England Journal of Medicine* (1995). 333: 1528-1533.
  36. Fernandez-Cruz, E., Lange, J.M., Frissen, J., Fumer, V., Chateauvert, M., Boucher, C.A., Dowd, P., and Stevens, J. Zidovudine plus interferon-alpha versus zidovudine alone in HIV-infected symptomatic or asymptomatic persons with CD4+ cell counts > 150 x 10 (6)/L: results of the Zidon trial. Zidon Study Group. *AIDS* (1995) 9,9:1025-35.
  37. Ingrand, D., Weber, J., Boucher, C.A., Loveday, C., Robert, C., Hill, A., and Cammack, N.

Phase I/II study of 3TC (lamivudine) in HIV-positive, asymptomatic or mild AIDS related complex patients: sustained reduction in viral markers. The Lamivudine European HIV Working Group. *AIDS* (1995) 9, 12: 1323-9.

38. Leeuwen, R. van, Katlama, C., Kitchen, V., Boucher, C.A.B., Tubiana, R., McBride, M., Didier, I., Weber, J., Hill, A., McDade, H. and Danner, S.A. Evaluation of safety and efficacy of 3TC (Lamivudine) in patients with asymptomatic or mildly symptomatic human immunodeficiency virus infection: A phase I/II study. *J. Infect. Dis.* (1995) 171:1166-71.
39. Nijhuis, M., Boucher, C.A.B., Schuurman, R. Sensitive procedure for the Amplification of HIV-1 RNA Using a Combined Reverse-Transcription and Amplification Reaction. *Biotechniques* (1995) 19,2:178-8,182.
40. Reedik, M., Boucher, C.A.B., Bommel, T. van, Ho, D.D., Tzeng, T.B., Sereni, D., Veyssier, P., Jurriaans, S., Granneman, R., Hsu, A., Leonard, J.M. and Danner, S.A. Safety, pharmacokinetics, and antiviral activity of A77003, a C<sub>2</sub> symmetry-based human immunodeficiency virus protease inhibitor. *Antimicrobial Agents and Chemotherapy* (1995) 39,7:1559-64.
41. Schuurman, R., Nijhuis, M., Leeuwen van, R., Schipper, P., Collis, P., Danner, S.A., Mulder, J., Loveday, C., Christopherson, C., Kwok, S., Sninsky, J., Boucher, C.A.B. Rapid changes in HIV-1 RNA load and appearance of drug resistance mutations in individuals treated with 3TC (lamivudine). *J. Infect. Dis.* (1995) 171:1411-9.
42. Veenstra, J., Schuurman, R., Cornelissen, M., Wout, A.B. van 't, Boucher, C.A.B., Schuitemaker, H., Goudsmit, J. and Coutinho, R.A. Transmission of zidovudine-resistant human immunodeficiency virus type 1 variants following deliberate injection of blood from a patient with AIDS: Characteristics and natural history of the virus. *Clinical Infectious diseases* (1995) 21,3:556-60.
43. Back, N.K.T., Nijhuis, M., Keulen, W., Boucher, C.A.B., Oude Essink, B.B., Kuilenburg, A.B.P., Van Gennip, A.H. and Berkhout, B. Reduced replication of 3TC-resistant HIV-1 variants in primary cells due to a processivity defect of the reverse transcriptase enzyme. *The EMBO Journal* (1996) 15,15:4040-49.
44. Boucher CA. An interview with Charles A.B. Boucher, MD, PhD. Interview by Mark Mascolini. *J Int Assoc Physicians AIDS Care*. 1995 Nov;1(10):30-5.
45. Been-Tiktak, A.M., Williams, I., Vreken, H.M., Richens, J., Aldam, D., Van Loon, A.M., Loveday, C., Boucher, C.A.B., Ward, P., Weller, I.V.D., and Borleffs, J.C.C. Safety, tolerance and efficacy of atevirdine in asymptomatic HIV-infected individuals. *AAC* (Nov. 1996) 2664 - 2668.
46. De Boer, R.J., Boucher, A.B. Anti-CD4 therapy for AIDS suggested by mathematical models. *Proc.R. Soc. Lond. B* (1996) 263:899-905.
47. Boucher, C.A.B., and Reedik, M. Viral resistance: a major challenge in managing HIV disease. *J. of Biol. Reg. and Homeostatic Agents* (1996) 9,3: 91-4.
48. Boucher, C.A.B., Keulen, W., Van Bommel, T., Nijhuis, M., De Jong, D., De Jong, M.D., Schipper, P., and Back, N.K.T. Human immunodeficiency virus type 1 drug susceptibility determination by using recombinant viruses generated from patient sera tested in a cell-killing assay. *AAC* (1996) 40,10:2404-09.
49. Boucher, C. Rational approaches to resistance: using saquinavir. *AIDS* (1996) vol.10

(suppl 1):S15-S19.

50. Boucher, C.A.B. Individualisation of HIV therapy based on HIV RNA load: the virologist's perspective. *Int J of Antimicrobial Agents* (1996) 7:211-215.
51. Carr, A., Vella, S., De Jong, M.D., Sorice, F., Imrie, A., Boucher, C.A., and Cooper, D.A. for the Dutch-Italian-Australian Nevirapine Study Group. A controlled trial of nevirapine plus zidovudine versus zidovudine alone in p24 antigenaemic HIV-infected patients. *AIDS* (1996) 10:635-41.
52. Frissen, J.P.H., Brinkman, K., Ten Napel, C.H.H., Ende, I.M.E.van der, Buuren, I.A.H.J.A.M. van, Boucher, C.A.B., Reiss, P., and Lange, J.M.A. Tolerability and activity of a new recombinant interferon- B/D hybrid in patients with HIV infection. *Antiviral Therapy* (1996) 1,2:89-97.
53. Jong, M.D. de, Schuurman, R., Lange, J.M.A., Boucher, C.A.B. Replication of a pre-existing resistant HIV-1 subpopulation in vivo after introduction of a strong selective drug pressure. *Antiviral Therapy* (1996) 1,1:33-41.
54. De Jong, M.D., Veenstra, J., Stilianakis, N.I., Schuurman, R., Lange, J.M.A., De Boer, R.J. and Boucher, C.A.B. Host-parasite dynamics and outgrowth of virus containing a single K70R amino acid change in reverse transcriptase are responsible for the loss of human immunodeficiency virus type 1 RNA load suppression by zidovudine. *Proc. Natl. Acad. Sci. USA* (1996) 93:5501-5506.
55. de Jong, M.D., Veenstra, J., Schuurman, R., Lange, J.M.A. and Boucher, C.A.B. Loss of HIV-1 RNA load response during zidovudine treatment coincides with the appearance of a single RT mutation at codon 70. *Proc. Natl Acad Science.* (1996). 93:5501-5506.
56. De Jong, M.D., Boucher, C.A.B., Galasso, G.J., Hirsch, M.S., Kern, E.R., Lange, J.M.A., and Richman, D.D. Consensus symposium on combined antiviral therapy *Antiviral Research* (1996) 29:5-29.
57. Keulen, W., Boucher, C.A.B. and Berkhout, B. Nucleotide substitution patterns can predict the requirements for drug-resistance of HIV-1 proteins. *Antiviral Research* (1996) 31:45-57.
58. Molla, A., Komeyeva, M., Gao, Q., Vasavanonda, S., Schipper, P.J., Mo, H-M., Markowitz, M., Chernyavskiy, T., Niu, P., Lyons, N., Hsu, A., Granneman, G.R., Ho, D.D., Boucher, C.A.B., Leonard, J.M., Norbeck, D.W., and Kempf, D.J. Ordered accumulation of mutations in HIV protease confers resistance to ritonavir. *Nature Medicine* (1996) 2,7:760-766.
59. Ronde, A. de, Schuurman R., Goudsmit J., Hoek, A.van den and Boucher, C.A.B. First case of new infection with zidovudine-resistant HIV-1 among prospectively studied intravenous drug users and homosexual men in Amsterdam, the Netherlands. *AIDS* (1996) 10(2): 231-232.
60. Schuurman, R., Descamps, D., Weverling, G.J., Kaye, S., Tijnagel, J., Williams, I., Van Leeuwen, R., Tedder, R., Boucher, C.A.B., Brun-Vezinet, F., and Loveday, C. Multicenter comparison of three commercial methods for HIV-1 RNA quantification in plasma. *J. Clin. Microbiol.* (1996) Dec.: 3016 - 3022.
61. Staszewski, S., Miller, V., Kober, A., Colebunders, R., Vandercam, B., Delesclust, J., Clumeck, N., Van Wanzeele, F., De Brabander, M., De Cree, J., Moeremans, M., Andries, K., Stoffels, P., Janssen, P.A.J., and members of the Loviride Collaborative

- Study Group. Evaluation of the efficacy and tolerance of R 018893, R 089439 (loviride) and placebo in asymptomatic HIV-1 infected patients. *Antiviral Therapy* (1996) 1,1:42-50.
62. Van 't Wout, A.B., De Jong, M.D., Kootstra, N.A., Veenstra, J., Lange, J.M.A., Boucher, C.A.B. and Schuitemaker, H. Changes in cellular load and zidovudine resistance of syncytium inducing and non-syncytium inducing human immunodeficiency virus populations under zidovudine pressure: a clonal analysis. *Journal of Infectious Diseases* (1996) 174 (4):845-849.
  63. Keulen W, Nijhuis M, Schuurman R, Berkhout B, Boucher C. Reverse transcriptase fidelity and HIV-1 variation. *Science*. 1997 Jan 10;275(5297):229; author reply 230-1.
  64. Been-Tiktak, A.M.M., de Haas, C.J.C., de Graaf, L., Boucher, C.A.B., Verhoef, J., Borleffs, J.C.C., Nottet, H.S.L.M., and Schuurman, R. In-vitro selection of HIV-1 variants resistant to non-nucleoside reverse transcriptase inhibitors in monocyte-derived macrophages. *Journal of Antimicrobial Chemotherapy*. (1997). 40: 847-853.
  65. Borleffs, J.C.C., Esseveld, F., Hoepelman, I.M., Boucher, C.A.B. AIDS, nieuwe ontwikkelingen. Behandeling van HIV-infectie. *Nederlands Tijdschrift voor Geneeskunde*. (1997). 14: 19-27.
  66. Van Leeuwen, R., Lange, J.M.A., Nijhuis, M., Schuurman, R., Relss, P., Danner, S.A., and Boucher, C.A.B. Results of long-term follow-up of HIV infected patients treated with lamivudine (3TC) monotherapy, followed by a combination of 3TC and zidovudine (ZDV). *Antiviral Therapy* (1997) 2 (2):79-90.
  67. Borleffs, J.C.C., Esseveld, F., Hoepelman, I.M., Boucher, C.A.B. AIDS; nieuwe ontwikkelingen II. Behandeling van HIV-infectie. *Nederlands Tijdschrift voor Geneeskunde*. (1997). 141: 1037-1043.
  68. Borleffs, J.C.C., Boucher, C.A.B., Bravenboer, B., Burger, D., Cohen, J.S., Hoetelmans, R., Juttmann, J., Koopmans, P., Koot, M., Kroon, F., van Leusen, R., Meenhorst, P., Roos, M., Schuurman, R., Sprenger, H., Waalberg, E. Saquinavir-Soft Gelatine Capsules versus Indinavir as Part of AZT and 3TC Containing Triple Therapy. *Journal of Clinical Infectious Diseases*. (1997). 25: 369-399.
  69. Boucher, C.A.B. Resistance development to proteinase inhibitors. *Hellenic Archives of AIDS*. (1997). 5: 19-23.
  70. Boucher, C.A.B. Antiviral drug resistance and cross-resistance. *Antiviral Therapy* (1997) 2(Supplement 3):19-23
  71. Brun-Vezinet, F., Boucher, C.A.B., Loveday, C., Descamps, D., Fauveau, V., Izopet, J., Jeffries, D., Kaye, S., Kryzanowski, C., Nunn, A., Schuurman, R., Seigneurin, J.-M., Tamalet, C., Tedder, R., Weber, J., and Weverling, G.-J. HIV-1 viral load, phenotype and resistance in a subset of drug-naïve participants from the Delta trial. *The Lancet* (1997) 350 (9083): 983-990.
  72. Burger, D.M., Boucher, C.A.B., Meenhorst, P.L., Kraaijeveld, C.L., Portegies, P., Mulder, J.W., Hoetelmans, R.M.W. HIV-1 RNA levels in the cerebrospinal fluid may increase owing to damage to the blood-brain barrier. *Antiviral Therapy*. (1997)2: 113-117.
  73. Coll, O., Hernandez, M., Boucher, C.A.B., Fortuny, C., de Tejada, B.M., Canet, Y., Caragol, I., Tijnagel, J., Bertran, J.M. and Español, T. Vertical HIV-1 transmission correlates with a high maternal viral load at delivery. *Journal of AIDS and Human Retrovirology* (1997) 14 (1):26-30.



74. De Jong, M.D., Carr, A., Vella, S., Boucher, C.A.B., Weverling, G.J., Imrie, A., French, S., Sorice, S., Pauluzzi, S., Chiodi, F., Van der Ende, M.E., Frissen, Ph.J., Weigel, H.M., Kauffmann, R.H., Lange, J.M.A., Yoon, R., Moroni, M., Hoeders, E., Leitz, G., Cooper, D.A., Hall, D., and Reiss, P. High dose nevirapine in previously untreated HIV-1 infected persons does not result in sustained suppression of HIV-1 replication. *Journal of Infectious Diseases* (1997) 175 (4): 966-970.
75. de Jong, M.D., Boucher, C.A.B., Cooper, D.A., Galasso, G.J., Gazzard, B., Lange, J.M.A. Summary of the II international consensus symposium on combined antiviral therapy and implications for future therapies. *Antiviral Research*. (1997). 35: 65-82.
76. De Jong, M.D., De Boer, R.J., De Wolf, F., Foudraine, N., Boucher, C.A.B., Goudsmit, J., and Lange, J.M.A. Transient overshoot of HIV-1 viraemia after early discontinuation of antiretroviral treatment: role of increased target cell availability? *AIDS* (1997) 11(11): F79-84.
77. Keulen, W., Van Wijk, A., Back, N.K.T., Boucher, C.A.B. and Berkhout, B. The initial appearance of the 184 Ile variant in 3TC-treated patients is due to the mutational bias of the HIV-1 reverse transcriptase. *Journal of Virology* (1997) 71 (4):3346-3350.
78. Keulen, W., Nijhuis, M., Schuurman, R., Berkhout, B. and Boucher, C. Increase in RT fidelity observed with the 184Val RT enzyme is not sufficient to prevent the generation of double resistant HIV-1 viruses. *Science* (1997) 275 (5297): 229.
79. van Leeuwen, R., Lange, J.M.A., Nijhuis, M., Schuurman, R., Reiss, P., Danner, S.A. and Boucher, C.A.B. Results of longterm follow-up of HIV infected patients treated with lamivudine monotherapy, followed by a combination of lamivudine and zidovudine. *Antiviral therapy* (1997). 2: 79-90.
80. Lehner, T., Biberfeld, P., Boucher, C.A.B., Darbyshire, J. Fenyö, Heeney, J.L., Jager, J.C., Lundgren, J.D., Newell, M.L., Rösch, P., Rossi, P. and Virelizier, J.L. European contribution to the science, prevention and management of HIV infection. *Vaccine* (1997) Vol. 15 No. 5: 465-468.
81. Miller, V., Staszewski, S., Boucher, C.A.B., and Phair, J.P. Clinical experience with non-nucleoside reverse transcriptase inhibitors. *AIDS* (1997), 11 (suppl. A): S157-S164.
82. Nijhuis, M., Schuurman, R., Boucher, C.A.B. Homologous recombination for rapid phenotyping of HIV. *Current Opinion in Infectious Diseases* 1997, 10:475-479.
83. Nijhuis, M., Schuurman, R., De Jong, D., Van Leeuwen, R., Lange, J., Danner, S., Keulen, W., De Groot, T., and Boucher, C.A.B. Lamivudine resistant HIV-1 variants (M184V) require multiple amino acid changes to become co-resistant to zidovudine in vivo. *Journal of Infectious Diseases* (1997) 176:398-405..
84. Stilianakis, N., Boucher, C.A.B., De Jong, M.D., Van Leeuwen, R., Schuurman, R., and De Boer, R.J. Clinical data sets of HIV-1 reverse transcriptase-resistant mutants explained by a mathematical model. *Journal of Virology* (1997) Jan.: 161-168.
85. van 't Wout, A.B., Ran, L.J., de Jong, M.D., Bakker, M., van Leeuwen, R., Notermans, D.W., Loeliger, A.E., de Wolf, F., Danner, S.A., Reiss, P., Boucher, C.A.B., Lange, J.M.A., & Schuitemaker, H. (in press). Selective inhibitions of SI and NSI HIV-1 variants by ddI and ZDV, respectively, may contribute to the enhanced clinical benefit of ZDV/ddI combination therapy. *Journal of Clinical Investigation* (1997) 100 (9): 2325-2332.

86. de Boer, R.J., Boucher, C.A.B., & Perelson, A.S. 1998. Target Cell Availability and the Successful Suppression of HIV by Hydroxyurea and Didanosine. *AIDS*, 12:1567-1570.
87. Brinkman, K., Huysmans, F., Schuurman, R., Boucher, C., and Koopmans, P. HIV viral load during anti-rejection therapies in a HIV infected kidney transplant recipient. *Lancet* (1998) 352 (9138): 1446.
88. Brinkman, K., Huysmans, F., Galama, J.M., Boucher, C.A.B. In-vivo anti-CD3-induced HIV-1 viraemia (letter). *The Lancet* (1998) 352 (9138): 1446
89. Bruisten, S., Reiss, P., Loeliger, A., Swieten, P. van, Schuurman, R., Boucher, C., Weverling, G., Huisman, J. Cellular proviral HIV type 1 DNA load persists after long-term RT-inhibitor therapy in HIV type 1 infected persons. *AIDS Research and Human Retroviruses* (1998) 14 (12): 1053-1058.
90. Cohen Stuart, J.W.T., Slieker, W.A.T., Rijkers, G.T., Noest, A., Boucher, C.A.B., Suur, M.H., de Boer, R., Geelen, S.P.M., Scherpbier, H., Hartwig, N.G., Hooijkaas, H., Roos, M.T., de Graeff-Meeder, B., & de Groot, R. Early recovery of CD4+ T lymphocytes in children on highly active antiretroviral therapy. *AIDS*, 12, 2155-2159, 1998.
91. Cohen Stuart, J.W.T., Boucher, C.A.B., Roos, M., Midema, F., Borleffs, J.C.C., Hamann, D. Toename van het aantal naieve CD8+ T-cellen in het bloed tijdens krachtige antiretrovirale therapie. *Nederlands Tijdschrift voor Geneeskunde*. (1998). 142: 2230-2231.
92. Cohen Stuart, J.W.T., Borleffs, J.C.C., Boucher, C.A.B., Schuurman, R., Langebeek, N., Richter, C., ter Hofstede, H., Burger, D., Koopmans, P.P., Zomer, B., Hamann, D., Roos, M.Th., van der Meulen, P., Sprenger, H., Dorama, W., Kroon, F.P., Bravenbroer, B., Juttmann, J.R., van der Ven, B., van Belle, L., Hoetelmans, R., Meenhorst, P., Waalberg, E.P. Comparative study of saquinavir soft-gel-capsule vs indinavir as part of triple therapy regimen (CHEESE study). *AIDS*. 12 (4): S14.
93. Cohen Stuart, J.W., Boucher, C.A., Cooper, D.A., Galasso, G.J., Richman, D.D., Thomas, H.C., Whitley, R.J. Summary of the III International Consensus Symposium on Combined Antiviral Therapy. *Antiviral. Res.* (1998). 38 (2): 75-93.
94. Cohen Stuart, J.W.T., Boucher, C.A., Roos, M., Miedema, F., Borleffs, J.C., Hamman, D. Increased serum level of naive CD8+ T cells during intensive antiretroviral therapy. *Nederlands Tijdschrift voor Geneeskunde*. (1998). 142 (40): 2230-1.
95. de Jong, M.D., Boucher C.A.B., Danner S.A., Gazzard B., Griffiths P.D., Katlama C., Lange J.M.A., Richman D.D., Vella S. Summary of the international consensus symposium on management of HIV, CMV and hepatitis virus infections, *Antiviral Research* 37(1998)1: 1-16.
96. Kempf, D.J., Rode, R.A., Xu, Y., Sun, E., Heath-Chiozzi, M.E., Valdes, J., Japour, A.J., Danner, S., Boucher, C., Molla, A., & Leonard, J.M. The duration of viral suppression during protease inhibitor therapy for HIV-1 infection is predicted by plasma HIV-1 RNA at the nadir. *AIDS*. 12, F9-F14, 1998.
97. Nijhuis, M., Boucher, C.A.B., Schipper, P., Leitner, T., Schuurman, R., & Albert, J. Stochastic processes strongly influence HIV-1 evolution during suboptimal protease inhibitor therapy. *Proceedings National Academy of Science USA*, 95, 14441-14446, 1998.
98. Orendi, J.M., Bloem, A.C., Borleffs, J.C.C., Wijnholds, F., de Vos, N.M., Nottet, H.S.L.M.,

- Visser, M.R., Snippe, H., Verhoef, J., & Boucher, C.A.B. 1998. Activation and cell cycle antigens in CD4+ and CD8+ T cells correlating with plasma human immunodeficiency virus (HIV-1) RNA level in HIV infection. *Journal of Infectious Diseases* (1998) 178 (5): 1279-1287.
99. Orendi, J.M., Boer, K., van Loon, A.M., Borleffs, J.C.C., van Oppen, A.C.C., & Boucher, C.A.B. Verticale HIV-1 transmissie: I. Risico en preventie bij de zwangere. *Nederlands Tijdschrift voor Geneeskunde*, 142, 2720-2724, 1998.
  100. Orendi, J.M., Geelen, S.P.M., de Graeff-Meeder, E.R., van Loon, A.M., Schuurman, R., & Boucher, C.A.B. Verticale HIV-1 transmissie:II. HIV-diagnostiek bij het kind. *Nederlands Tijdschrift voor Geneeskunde*, 142, 2724-2728, 1998.
  101. Ruiz L., Nijhuis M., Boucher C., Puig T., Bonjoch A., Martínez-Picado J., Marfil S., de Jong D., Burger D., Arnó A., Balagué M., Clotet B. Efficacy of adding indinavir to previous reverse transcriptase nucleoside analogues in relation to genotypic and phenotypic resistance development in advanced HIV-1-infected patients. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 1998, 19:19-28
  102. Van 't Wout A.B., Ran L.J., Nijhuis M., Tijnagel J.M.G.H., de Groot T., van Leeuwen R., Boucher C.A.B., Schuitemaker H., Schuurman R. Efficient inhibitor of both syncytium-inducing and non-syncytium-inducing wild-type HIV-1 by lamivudine *in vivo*. *AIDS* 1998, 12:1169-1176.
  103. Orendi JM, Boer K, van Loon AM, Borleffs JC, van Oppen AC, Boucher CA. Vertical HIV-I-transmission. I. Risk and prevention in pregnancy. *Ned Tijdschr Geneesk*. 1998 Dec 12;142(50):2720-4.
  104. Orendi JM, Geelen SP, de Graeff-Meeder ER, van Loon AM, Schuurman R, Boucher CA. Vertical HIV-I-transmission. II. HIV-diagnosis in a child. *Ned Tijdschr Geneesk*. 1998 Dec 12;142(50):2724-8.
  105. van 't Wout, A.B., Ran, L.J., de Jong, M.D., Bakker, M., van Leeuwen, R., Notermans, D.W., Loeliger, A.E., de Wolf, F., Danner, S.A., Reiss, p., boucher, C.A.B., Lange, J.M.A. & Schuitemaker, H. (in press). Selective inhibitions of SI and NSI HIV-1 variants by ddI and ZDV, respectively, may contribute to the enhanced clinical benefit of ZDV/ddI combination therapy. *Journal of Clinical Investigation*.
  106. Been-Tiktak, A.M.M., Boucher, C.A.B., Brun-Vézinet, F., Joly, V., Mulder, J.W., Jost, J., Cooper, D.A., Gatell, J.M., Staszewski, S., Colebunders, R., Stewart, G.J., Hawkins, D.A., Johnson M.A., Parkin, J.M., Kennedy, D.H., Hoy, J.F., Borleffs, J.C. Efficacy and safety of combination therapy with delavirdine and zidovudine: a European/Australian phase II trial. *Int. J. of Antimicrobial Agents*. (1999). 11: 13-21.
  107. Boucher, C.A.B. HIV drug resistance tests are here to stay. *Current opinion in Infectious Diseases*. (1999). 12: 27-32.
  108. Cohen Stuart, J.W., Schuurman, R., Burger, D.M., Koopmans, P.P., Sprenger, H.G., Juttmann, J.R., Richter, C., Meenhorst, P.L., Hoetelmans, R.M., Kroon, F.P., Bravenboer, B., Hamann, D. Boucher, C.A., Borleffs, J.C. Randomized trial comparing saquinavir soft gelatin capsules versus indinavir as part of triple therapy. *AIDS*. (1999). 13 (7): F53-8.
  109. Durant J, Clevenbergh P, Halfon P, Delgiudice P, Porsin S, Simonet P, Montagne N, Boucher CA, Schapiro JM, Dellamonica P. Drug-resistance genotyping in HIV-1 therapy: the VIRADAPT randomised controlled trial. *Lancet* 1999 June 26;353(9171):2173-4.

110. Durant, J., Clevenbergh, P., Halfon, P., Delguidice, P., Porsin, S., Simonet, P., Montagne, N., Dohin, E., Schapiro, J.M., Boucher, C., Dellamonica, P. Improving HIV therapy with drug resistance genotyping: The Viradapt Study. *Lancet* 1999; 353:2195-2199.
111. Kamp, W., Schokker, J., Cambridge, E., de Jong, S., Schuurman, R., de Groot, T., Boucher, C. Effect of Weekly adefovir (PMEA) infusions on HIV-1 virus load: results of a phase I/II study. *Antiviral Therapy* 1999; 4:101-107.
112. Keulen, W., van Wijk, A., Schuurman, R., Berkhout, B., Boucher, C.A.B. Increased polymerase fidelity of lamivudine resistant HIV-1 variants does not limit their evolutionary potential. *AIDS*. (1999). 13: 1343-1349.
113. Nijhuis, M., Schuurman, R., de Jong, D., Erickson, J., Gustchina, E., Albert, J., Schipper, P., Gulnik, S., Boucher, C.A.B. Increased fitness of drug resistant HIV-1 protease as a result of acquisition of compensatory mutations during suboptimal therapy. *AIDS*. (1999). 13: 2349-2359.
114. Orendi, J.M., Boer, K., van Oppen, A.C., Borleffs, J.C., van Loon, A.M., Boucher, C.A.B. Verticale HIV-1 transmissie. Risico en preventie bij de zwangere [letter]. *Nederlands Tijdschrift Geneeskunde*. (1999). 143: 435-436.
115. Pembrey, L., Newell, M.L., Tovo, P.-A. European Paediatric Hepatitis C Virus Network. Antenatal hepatitis C virus screening and management of infected women and their children: policies in Europe. *European Journal of Pediatrics* 1999; 158: 842-846.
116. Schuurman, R., Demeter, L., Reichelderfer, P., Tijnagel, J., de Groot, T., Boucher, C.A. Worldwide evaluation of DNA sequencing approaches for identification of drug resistance mutations in the human immunodeficiency virus type 1 reverse transcriptase. *Journal of Clinical Microbiology*. (1999). 37 (7): 2291-2296.
117. Hazenberg MD, Stuart JW, Otto SA, Borleffs JC, Boucher CA, de Boer RJ, Miedema F, Hamann D. T-cell division in human immunodeficiency virus (HIV)-1 infection is mainly due to immune activation: a longitudinal analysis in patients before and during highly active antiretroviral therapy (HAART). *Blood*. 2000 Jan 1;95(1):249-55.
118. Back, N.K.T., van Wijk, A., Remmerswaal, D., van Montfort, M., Nijhuis, M., Schuurman, R., and Boucher, C.A. In vitro tipranavir susceptibility of HIV-1 isolates with reduced susceptibility to other protease inhibitors. *AIDS*. (2000). 14 (1): 101-102.
119. P.Clevenbergh, J. Durant, P. Halfon, P. del Giudice, V. Mondain, N. Montagne, J.M. Schapiro, C.A.B. Boucher and P. Dellamonica - Persisting long-term benefit of genotype-guided treatment for HIV-infected patients failing HAART. The Viradapt study: week 48 follow up. *Antiviral Therapy* (2000), 5: 65-70.
120. Orendi JM, Nottet HS, De Vos NM, Visser MR, Snippe H, Boucher CA, Verhoef J. Hydroxyurea interferes with antigen-dependent T-cell activation in vitro. *Eur J Clin Invest*. 2000 Feb;30(2):162-6.
121. European Paediatric Hepatitis C Virus Infection Network, Tovo, P.-A., Pembrey, L.J. and Newell, M-L.. Persistence Rate and Progression of Vertically Acquired Hepatitis C Infection. *The Journal of Infectious Diseases* (2000). 181: 419-24.
122. Hazenberg, M.D., Otto, S.A., Cohen Stuart, J.W.T., Verschuren, M.C.M., Borleffs, J.C.C., Boucher, C.A.B., Coutinho, R.A., Lange, J.M.A., Rinke de Wit, T.F., Tsegaye, A., van Dongen, J.M. van, Hamann, D., de Boer, R.J., Miedema, F. Increased cell division but not

- thymic dysfunction rapidly affects the T-cell receptor excision circle content of the naive T cell population in HIV-1 infection. *Nature Medicine*, 2000, september, 6 (8), 1036-1042
123. Cohen Stuart JW, Hazebergh MD, Hamann D, Otto SA, Borleffs JC, Miedema F, Boucher CA, de Boer RJ. The dominant source of CD4+ and CD8+ T-cell activation in HIV infection is antigenic stimulation. *J Acquir Immune Defic Syndr*. 2000 Nov 1;25(3):203-11.
  124. L.J.R. van Elden, G.A. van Essen, C.A.B. Boucher, M. Nijhuis, A.M. van Loon, - Nieuwe antivirale middelen voor de preventie en behandeling van influenza. *Nederlands Tijdschrift voor Medische Microbiologie*, 8<sup>e</sup> jaargang, december 2000, no. 4, 124-128.
  125. Para. Michael, F. , David V. Glidden, Robert W. Coombs, Ann. C. Collier, John H. Condra, Charles Craig, Roland Bassett, Randi Leavitt. Baseline Human Immunodeficiency Virus Type 1 Phenotype, Genotype, and RNA Response after Switching from Long-Term Hard-Capsule Saquinavir to Indinavir or Soft-Gel-Capsule Saquinavir in AIDS Clinical Trials Group Protocol 333, *The Journal of Infectious Diseases*, 2000; 182; 733-43
  126. Marée, A.F.M., Keulen, W., Boucher, C.A.B., Boer, R.J. de. Estimating Relative Fitness in Viral Competition Experiments. *Journal of Virology* (2000), december, 74 (23) : 11067-11072
  127. Sevin, A.D., DeGruttola, Nijhuis, M., Schapiro, J.M., Foulkes, A.S., Para, M.F., Boucher, C.A.B. Methods for Investigation of the Relationship between Drug-Susceptibility Phenotype and Human Immunodeficiency Virus Type 1 Genotype with Applications to AIDS Clinical Trials Group 333. *The Journal of Infectious Diseases*, (2000) 182 : 59-67
  128. Vaerenbergh, Kristien van, Kristel van Laethem, Jan Albert, Charles, A.B. Boucher, Bonaventura Clotet, Marco Floridia, Jan Gerstoft, Bo Heideman, Claus Nielsen, Christophe Pannecouqou, Luc Perrin, Maria F. Pirillo, Lidia Ruiz, Jean-Claude Schmit, François Schneider, Anne Schoolmeester, Rob Schuurman, Hans J. Stellbrink, Lieven Stuyver, Jan van Lunzen, Barbara van Remoortel, Eric van Wijngaerden, Stefano Vella, Myriam Witvrouw, Sabine Yerley, Erik de Clercq, Jan Desmyter, Anne-Mieke Vandamme. Prevalence and Characteristics of Multinucleoside-Resistant Human Immunodeficiency Virus Type 1 among European Patients Receiving Combinations of Nucleoside Analogues. *Antimicrobial Agents and Chemotherapy*, Aug. 2000, p. 2109-2117.
  129. Frost SD, Nijhuis M, Schuurman R, Boucher CA, Brown AJ. Evolution of lamivudine resistance in human immunodeficiency virus type 1-infected individuals: the relative roles of drift and selection. *J Virol*. 2000 (14):6262-6268.
  130. Mascolini M, Wensing AM, Boucher CA. HIV resistance assay results and their effect on therapeutic decisions. *AIDS*. 2001 Jan 5;15(1):124-6.
  131. Monique Nijhuis, Steven Deeks, Charles Boucher - Implications of antiviral resistance on viral fitness. *Current Opinion in Infectious Diseases*, 2001, 14:23-28.
  132. The EuroGuidelines Group for HIV Resistance. Clinical and laboratory guidelines for the use of HIV-1 drug resistance testing as part of treatment management: recommendations for the European setting. *AIDS* (2001) 15(3) p. 309-320.
  133. Joost W.J. van Esser, Hubert G.M. Niesters, Steven F.T. Thijsen, Ellen Meijer, Albert D.M.E. Osterhaus, Katja C. Wolthers, Charles A.B. Boucher, Jan Willem Gratama, Leo M. Budel, Bronno van der Holt, Anton M. van Loon, Bob Löwenberg, Leo F. Verdonck and Jan J. Cornelissen. Molecular quantification of viral load in plasma allows for fast and accurate prediction of response to therapy of Epstein-Barr virus-associated lymphoproliferative disease after allogeneic stem cell transplantation. *British Journal of*

*Haematology* (2001), 113, 814-821.

134. Rienk E. Jeeninga, Wilco Keulen, Charles A.B. Boucher, Rogier W. Sanders and Ben Berkhout. Evolution of AZT Resistance in HIV-1: The 41-70 intermediate that is not observed in vivo has a replication defect. *Virology* (2001), 283, 294-305.
135. James W.T. Cohen Stuart, Annemarie M.J. Wensing, Colin Kovacs, Maïke Righart, Dorien de Jong, Steve Kaye, Rob Schuurman, Corjan J.T. Visser and Charles Boucher. Transient Relapses ("Blips") of Plasma HIV RNA Levels During HAART Are Associated With Drug Resistance. *Journal of Acquired Immune Deficiency Syndromes* (2001) 28: 105-113.
136. Paediatric European Network for Treatment of AIDS (PENTA). Five year follow up of vertically HIV infected children in a randomised double blind controlled trial of immediate versus deferred zidovudine: the PENTA 1 trial. *Archives of Disease in Childhood*, March 2001, Vol. 84, No. 3, p. 230-236.
137. van Elden LJ, van Essen GA, Boucher CA, van Loon AM, Nijhuis M, Schipper P, Verheij TJ, Hoepelman IM. Clinical diagnosis of influenza virus infection: evaluation of diagnostic tools in general practice. *Br J Gen Pract.* 2001 Aug;51(469):630-4.
138. Wensing AM, Reedik M, Richter C, Boucher CA, Borleffs JC. Replacing zidovudine by zalcitabine or zalcitabine/saquinavir as part of highly active antiretroviral therapy leads to an improvement of triglyceride levels. *AIDS.* 2001 Nov 9;15(16):2191-3.
139. Peter Sloot, Fan Chen and Charles Boucher. Cellular Automata Model of Drug Therapy for HIV Infection. *ACRI 2002, LNCS 2493*, pp. 282-293, 2002.
140. Anita De Rossi, A. Saray Walker, Davide De Forni and Diana M. Gibb, on behalf of the Paediatric European Network for Treatment of AIDS (PENTA). Biphasic decay of cell-associated HIV-1 RNA in HIV-1-infected children on antiretroviral therapy. *AIDS* (2002), Vol. 16 issue 14, p. 1961-1963.
141. Maxeiner H.G., Keulen W. Schuurman R., Bijen M., de Graaf L., van Wijk A., Back N., Kline M.W., Boucher C.A., Nijhuis M. Selection of zidovudine resistance mutations and escape of human immunodeficiency virus type 1 from antiretroviral pressure in stavudine-treated pediatric patients. *J. Infectious Diseases* 2002 April 15 185(8):1070-6.
142. Schuurman R., Brambilla D., de Groot T., Huang D., Land S., Bremer J., Benders I., Boucher C.A. Underestimation of HIV type 1 drug resistance mutations: results from the ENVA-2 genotyping proficiency program. *AIDS Res. Hum. Retroviruses* 2002 March 1;18(4):243-8.
143. Tural C., Ruiz L., Holtzer C., Schapiro J., Viciano P., Gonzalez J., Domingo P., Boucher C., Rey-Joly C., Clotet B. Clinical utility of HIV-1 genotyping and expert advice: the Havana trial. *AIDS* 2002 January 25;16(2):209-18.
144. Cohen Stuart J, Hamann D, Borleffs J, Roos M, Miedema F, Boucher C, de Boer R. Reconstitution of naive T cells during antiretroviral treatment of HIV-infected adults is dependent on age. *AIDS.* 2002 Nov 22;16(17):2263-6.
145. Reddy Y.S., Kashuba A., Gerber J. and Miller V. on behalf of the roundtable participants. Importance of antiretroviral drug concentrations in sanctuary sites and viral reservoirs. *AIDS Research and human retroviruses* 2003 volume 19, number 3, pp 167-176.

146. J. Martinez-Picado, E. Negredo, L. Ruiz, C.R. Fumaz, A. Shintani, C. Zala, P. Domingo, J. Vilaro, J.M. Llibre, P. Viciano, K. Hertogs, C. Boucher, R.T. D'aquila, B. Clotet and the SWATCH Study Team. A Multi-center, randomized trial of proactive switching and alternation of antiretroviral drug regimens for HIV infection. *Ann Intern Med.* 2003;139:81-89.
147. Haverkamp M, Smit M, Weersink A, Boucher CA, Hoepelman AI. The effect of lamivudine on the replication of hepatitis B virus in HIV-infected patients depends on the host immune status (CD4 cell count). *AIDS.* 2003 Jul 4;17(10):1572-4.
148. Annemarie M.J. Wensing and Charles A.B. Boucher. Worldwide Transmission of Drug-resistant HIV. *Aids Reviews* July-September 2003; vol. 5 number 3: 140-155.
149. Torti C, Quiros-Roldan E, Keulen W, Scudeller L, Lo Caputo S, Boucher C, Castelli F, Mazzotta F, Pierotti P, Been-Tiktak AM, Buccoliero G, De Gennaro M, Carosi G, Tinelli C; GenPherex Study Group of the MaSTeR Cohort. Comparison between rules-based human immunodeficiency virus type 1 genotype interpretations and real or virtual phenotype: concordance analysis and correlation with clinical outcome in heavily treated patients. *J Infect Dis.* 2003 Jul 15; 188(2): 194-201. Epub 2003 Jul 01.
150. Aarnoutse RE, Schapiro JM, Boucher CA, Hekster YA, Burger DM. Therapeutic drug monitoring: an aid to optimising response to antiretroviral drugs? *Drugs.* 2003; 63(8): 741-53. Review.

## II Book chapters

Goudsmit, J., Lange, J.M.A. and Boucher, C.A.B. AIDS: een lentivirusinfectie bij de mens. *Bijblijven* (1988) 4,9:15-22.

Boucher, C.A.B. and Goudsmit, J. JOURNAL OF AIDS: a retrovirus infection in humans. In: *Diagnostic imaging of AIDS*, edited by Reenders, J.W.A.J. Stuttgart: Georg Thieme Verlag, 1992, p. 22-28.

Boucher, C.A.B. and Goudsmit, J. Humane immunodeficiëntievirussen. In: *Medische Virologie*, edited by Wilterdink, J.B. Houten/Antwerpen: Bohn, Stafleu & Van Loghum, 1992, p. 236-44.

Larder, B.A. and Boucher, C.A.B. PCR detection of human Immunodeficiency virus drug resistance mutations. In: Persing, D.H., Smith, T.F., Tenover, F.C. and White, T.J. (Eds), *Diagnostic molecular microbiology*. Principles and applications. American Society for Microbiology, Washington/Mayo Foundation, Rochester, M.N. 55905, 1993, pp 527-33.

Boucher C.A.B. HIV development of drug resistance. In : *H. Jaeger HIV-Medizin: Möglichkeiten der individualisierten Therapie; Wissenschaftlicher Ergebnisse in der Mitte der 90er Jahre*. Landsberg/Lech: ecomed, 1994, p. 41-4.

Boucher, C.A.B. Human Immunodeficiency Viruses and Human T-Lymphotropic Viruses. In: G.J. Galasso, R.J. Whitley, & T.C. Merigan (Eds.), *Antiviral Agents and Human Viral Diseases*. Philadelphia: Lippincott-Raven, 1997, p. 607-696.

Boucher C.A.B., Cohen Stuart J.W.T. De waarde van HIV-resistentiebepalingen voor de kliniek. *Pharmaceutisch Weekblad* 133 (1998)14: 572-577.

Boucher C.A.B., van Bergen J.E.A.M. Pathogenese: Immuunsysteem, Virusvermenigvuldiging, Pathogenese, Implicaties van de nieuwe inzichten voor de behandeling van de hiv-infectie. In: van Bergen J.E.A.M., Wigersma L., e.a. (red.) *De hiv-wijzer. Voor huisartsen en andere hulpverleners*, Amsterdam 1998.

Cohen Stuart, J.W.T. and Boucher, C.A.B. Human Retroviruses and Retroviral Infections. In: D. Armstrong & J. Cohen (Eds.) *Infectious Diseases*. Mosby, Harcourt Publishers Ltd., 1999, p. 10.1 - 10.10

Boucher, Ch. et al. Guide to Management of HIV Resistance and Pharmacokinetics of Drug Therapy (2000), First edition, Editorial TAISA, S.L., Provenca 192, Barcelona.

Boucher, Ch. et al. Guide to Management of HIV Resistance and Pharmacokinetics of Antiretroviral Therapy (2002), Second edition, Editorial TAISA, S.L., Provenca 192, Barcelona.

Boucher, Ch. et al. Guide to Management of HIV Resistance and Pharmacokinetics of Antiretroviral Therapy (2002), Third edition, Fundacio de Lluita contra la Sida, Hospital Universitari "Germans Trias i Pujol" 08916 Badalona, Catalonia.

Boucher C.A.B., Wensing A.M.J., Benders I.T.J.M. *Transmission of resistant viruses. HIV-Infect* N.H. Brockmeyer et al (ISBN 3-540-66478-5, 22-28)



---

### **III BOOKS**

**Editor of Practical Guidelines in Antiviral Therapy. Boucher C.A.B. and Galasso J. Elsevier publishers 2002.**

#### IV Other Publications & Editorials

Lelie, P.N., Poel van der, C.L., Reesink, H.W., Huisman, J.G., Boucher, C.A.B. and Goudsmit, J. Hoe effectief zijn de nieuwe-generatie antistof testen voor detectie van (vroeg) HIV-1 en HIV-2 infectie? *CLB bulletin* (1988) 7,3:1-3.

Boucher, C.A.B., Kellam, P., Tijnagel, J. and Larder, B.A. Evolution of zidovudine resistant HIV-1. *Int. Antivir. News* (1993), 1

Jong, M.de, Boucher, C.A.B. and Lange, J.M.A. Resistentie-ontwikkeling bij de antiretrovirale behandeling van een HIV-infectie. *Pharmaceutisch Weekblad* (1993) 128:331-35.

Artikel over Charles Boucher en zijn onderzoek in het AMC, *Folia* (1993, 15) 47:8.

Jong, M.de and Boucher, C.A.B. Syncytia formation and HIV load. *Transcript* (1993) 9-12.

Boucher, C.A.B. Viral load, phenotype and sensitivity. In: *Rocchi, G. (Ed.) Aspects of antiviral combination therapy in HIV management*. International Seminars Series. Colwood House Medical Publications (UK) Ltd, Berkshire, 1993, pag. 6-8.

Boucher, C.A.B. Viral resistance and replication: implications for drug development and patient management. *Antiviral Academy: Highlights of a symposium held May 12-13, 1995 in Paris, France, p 10-12* (Bristol Myers Squibb Company).

Boucher, C.A.B., and Merigan, T. Individualised therapy - implications for treatment. (1995) *Transcript* 40:12-15.

Boucher, C.A.B. More efficacious and sustained antiviral effects from combination versus monotherapy may result from changing patterns of drug resistance in HIV. *Transcript*. (1996). 44: 2-5.

Boucher, C.A.B. and Schuurman, R. Rapid changes in human immunodeficiency virus (HIV)-1 RNA load and appearance of drug resistant virus populations in individuals treated with 3TC (Lamivudine). *Antiviral News*. (1996). 4: 43-45.

Boucher, C.A.B. More efficacious and sustained antiviral effects from combination versus monotherapy may result from changing patterns of drug resistance in HIV. *Transcript* (ed. 44, March 1996) p. 2-5.

Boucher, Charles MD PhD and Saag, Michael MD, Viral Load in HIV Infection: Assays and Clinical Applications (educational series). *Adelphi Communications Ltd on behalf of F. Hoffmann-La Roche Ltd*. First Edition, June 1996.

Boucher, Charles and Pauwels, Rudi. Un cocktail preparato su misura. *Ricerca Roche*. No. 15, Marzo 1997.

Article based on an interview with Charles Boucher entitled 'Aids', *Vrij Nederland*, 51-52, p.32, 1997

Boucher, C.A.B. HIV-infecties en AIDS. *RIVM rapport "SOA in Nederland": hfdst 3 "Ziektebeeld, microbiologie, diagnostiek en behandeling"*, blz. 88. Update tot en met 1996. September 1997.

Boucher, C.A.B. Novel strategies in antiviral drug design. In: Novel strategies against pathogenic organisms. Proceedings of the 10th SB Kurhaus Workshop on Infectious Diseases. SmithKline Beecham Farma b.v. 1998, p. 105-108

- Boucher, C.A.B. Het mechanisme van HIV geneesmiddelenresistentie. Glaxo Wellcome. Interview with European AIDS Treatment News (EATNews) entitled *Combinations: Which and When?*, which appeared in Volume 5, number 3, 1996
- Monique Doppert: Het gevecht tegen resistentie. Grasduinen naar een AIDSremmer.
- Editor of the booklet "Het mechanisme van HIV geneesmiddelresistentie", 1998
- Co-editor of *Is it possible to eradicate HIV?* Madrid 1998, Fundació irsiCaixa.
- Boucher, Charles. Medicijnen helpen Afrika van de regen in de drup. (2000), Vrij Nederland, 14 oktober 2000, p. 19.
- Borleffs, J.C.C., Boucher, C.A.B. Dendritische cellen als koerier voor het humaan immunodeficientievirus (HIV). Ned. Tijdschrift voor Geneeskunde, 2000, apr. 22; 144 (17).
- Boucher C.A.B., B. Clotet, L. Menéndez-Arias, L. Ruiz, C. Tural, A. Van-Damme, D. Burger, J. Schapiro, R. D'Aquila, D. Richman. *Guide to management of HIV resistance and pharmacokinetics of drug therapy*. First Edition 2000. Edition coordination: Yolande Isabal, editorial TAISA, S.L.
- Boucher C.A.B., E.L.M. Op de Coul. RIVM rapport "SOA in Nederland": hfdst 8 "HIV infecties en AIDS", blz. 157-190. December 2000.
- Boucher, C.A.B., Aids, U-blad "Het Torentje", 10 mei 2001, p. 20
- Boucher C.A.B., A.M.J. Wensing, M. Mascolini. How testing for HIV resistance influences therapeutic decision making. IAPAC (May 2001) 7:3, p. 85-90.
- Jan C.C. Borleffs, Charles Boucher, Wendy Chaka, Sibyl P.M. Geelen, Babette E.R. de Graeff-Meeder, Andy I.M. Hoepelman. AIDS and PAIDS: Comparison of high-income countries and sub-Saharan countries like Zimbabwe. Growing up in pediatric immunology (a tribute to Professor Dr. Ben J.M. Zegers). Utrecht 2002. 125 - 133.
- Charles A.B. Boucher en Annemarie M.J. Wensing. Klinische toepassing en interpretatie van HIV resistentiebepalingen. Capita Selecta HIV/AIDS Van Zuiden communications 2002.
- Charles A.B. Boucher. U Blad d.d. 27 februari 2003 (jaargang 2 nummer 24) Het Torentje. *Aidsvaccin*.
- Editor of the Rapid Report of the XI International HIV Drug Resistance Workshop. Basic Principles & Clinical Implications. July 2-5, 2002 Seville, Spain.
- Bionieuws nr. 8 jaargang 13 d.d. 25-04-03 Antivirale Middelen – Als vaccineren te laat is. C.A.B. Boucher
- E.B. Fanoy, C.A.B. Boucher. Dieren op markten in China vormen mogelijk de bron van aan SARS gerelateerd virus. Ned Tijdschr Geneesk 2003, 8 november, 147(45): 2251.
- Charles A.B. Boucher. Scan van Februari 2004 (1/04). Therapietrouw blijft schild tegen resistentie – Aids-remmers voor Afrika.

## Lectures

- 89.01L Immune Deficiency Conference (University of Wisconsin, Madison), Madison, WI, USA, 6 September 1989  
*HIV-1 gag gene products: their expression during natural infection and presence of an HIV-1 neutralizing epitope*
- 90.01L Refereeravond Vakgroep Medische Microbiologie, Leiden, 2 mei 1990.  
*Gevoeligheidsbepaling van HIV voor AZT*
- 90.01L Ministerio de Sanidad y Consumo, Instituto de Salud Carlos III, Madrid, Spain, 4 May 1990  
*AZT resistance in asymptomatic individuals*
- 90.02L AIDS en beelddiagnostiek (Academic Medical Center), Amsterdam, the Netherlands, 30 May 1990  
*Virologie van AIDS*
- 90.03L 6th International conference on AIDS, San Francisco, CA, USA, 20-24 June 1990  
*Drug sensitivity and biological phenotype of serial HIV isolates from zidovudine treated asymptomatic individuals*
- 91.01L Antigenic and genetic variability of HIV-1 in Europe (Ministerio de Sanidad y Consumo, Instituto de Salud Carlos III; University of Amsterdam, Human Retrovirus Laboratory), Madrid, Spain, 13-14 June 1991  
*Biological and genetic resistance analysis in individuals on AZT treatment*
- 1.02L 7th International conference on AIDS, Florence, Italy, 16-21 June 1991  
*Zidovudine sensitivity of HIV during the development from the asymptomatic stage to AIDS*
- 91.03L Pediatric European Network for treatment in HIV infected children, Paris, France, 15-16 November 1991  
*HIV resistance of HIV infection to antiviral drugs*
- 91.04L Forum Huraux, Paris, France, November 1991  
*Clinical significance of zidovudine resistant human immunodeficiency viruses*
- 91.05L Bristol-Myers Squibb Antiviral Academy Meeting, Vienna, Austria, 1-2 November 1991  
*Diagnostic and virologic tools for clinical measurement of HIV*
- 91.06L Frontiers in HIV therapy. Fourth conference of the NIH National Cooperative Drug Discovery Groups for the Treatment of HIV Infection. J: Drug Resistance, San Diego, California, USA, 6 November 1991  
*HIV-1 biological phenotype rather than zidovudine sensitivity is associated with rapid clinical progression of asymptomatic individuals during treatment*
- 91.07L Seminar clinical research group, Boehringer Ingelheim Pharmaceuticals, Inc. New York, USA, 12-13 November 1991  
*Development of zidovudine resistant HIV-isolates in treated initially asymptomatic individuals*
- 91.08L International AIDS therapy group, Washington, DC, USA, 2 December 1991  
*HIV-1 biological phenotype, but not zidovudine resistance pattern is associated with*

*rapid clinical progression of asymptomatic individuals treated with zidovudine*

- 92.01L Workshop on viral drug resistance, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, US, 25 Februari 1992  
*Review of data from ZDV-treated patients*
- 92.02L Molecular Pathogenesis of HIV-1. Boehringer Ingelheim Pharmaceuticals Inc./Yale University, America, USA, 21-22 April 1992  
*Zidovudine resistance, virulence, and disease progression*
- 92.03L Second workshop on viral resistance, Washington DC, USA, 13-15 May 1992.  
*Genotypic assays, PCR*
- 92.04L Second workshop on viral resistance, Walter Reed Army Institute of Research/Food and Drug Administration, Washington DC, USA, 13-15 May 1992.  
*National history/clinical significance: Zidovudine and didanosine (ddI)*
- 92.05L Nevirapine Medical Conference, Boehringer Ingelheim, San Diego US, 12 June 1992  
*Effects of alternating therapy with zidovudine and nevirapine*
- 92.06L 8th International conference on AIDS, Amsterdam, the Netherlands, July 19-24 1992  
*HIV-1 phenotype rather than high level AZT resistance is associated with rapid clinical progression of asymptomatic treated patients*
- 92.07L 8th International conference on AIDS, Amsterdam, the Netherlands, July 19-24 1992  
*Evolution of zidovudine resistant HIV-1 isolates assessed by clonal analysis*
- 92.08L Meeting on prevention of the perinatal transmission of HIV by pharmacological and immunological means, Global Programme on AIDS, WHO, Geneva, Switzerland, 22-23 October 1992  
*Virological determinants of perinatal HIV transmission*
- 92.09L Act Up, New York NY, USA, 30 October 1992  
*Antiviral drug resistance on viral phenotype in relation to disease progression*
- 92.10L International Congress on Drug Therapy in HIV Infection, Glasgow, UK, 9-12 November 1992  
*In vitro selection of 3TC resistant HIV-1 isolates*
- 92.11L 3TC Virologists Meeting, MRC/Glaxo, 26 november 1992, London, UK  
*Resistance studies*
- 92.12L Nederlandse Vereniging voor Microbiologie, sectie Virologie/RIVM; Virologendag, Bilthoven, 8 December 1992  
*Antivirale therapie van HIV infecties*
- 92.13L HIV op de kindereleeftijd, the first Dutch conference on HIV-infections in children, Wilhelmina Kinderziekenhuis, Utrecht, 11 december 1992.  
*HIV Diagnostiek en therapie evaluatie*
- 92.14L Diagnostiek en therapie van infecties (University of Amsterdam), Amsterdam, the Netherlands 17 December 1992  
*Antiretrovirale therapie*
- 93.01L Vertical transmission intervention strategies, European collaborative study, 11-13 January 1993, London UK

*Summary of the WHO intervention workshop: chemotherapy*

- 93.02L Refereerbijeenkomst Medische Microbiologie, University of Amsterdam, 18 januari 1993  
*Antivirale Therapie*
- 93.04L ZIDON Investigator's meeting, Wellcome Research Laboratories, Beckenham, UK, 29 January 1993  
*ZIDON pilot study - review of zidovudine sensitivity data*
- 93.05L Workshop on primary HIV infection, NAID, NIH, Bethesda, USA, 25-26 February 1993  
*HIV-1 phenotypes in primary infection*
- 93.06L Workshop on primary HIV infection, NAID, NIH, Bethesda, USA, 25-26 February 1993  
*HIV-1 biological phenotype in relation to ZDV resistance and disease progression*
- 93.07L HIV: ontwikkeling van AZT-resistentie (microsymposium medische microbiologie, Academisch Ziekenhuis Nijmegen), Nijmegen, the Netherlands, 1 March 1993  
*Ontwikkeling van AZT resistente HIV varianten*
- 93.08L Aspects of antiviral combination therapy in HIV management (international seminar series: the management of HIV infection), Vienna, Austria, 12-14 March 1993  
*Viral load, phenotype and sensitivity*
- 93.09L Refereeravond Vakgroep Medische Microbiologie, Leiden, 24 maart 1993.  
*Zidovudine resistentie van HIV, fenotype en progressie*
- 93.10L Roche Molecular Systems, diagnostics research, Alameda, CA, USA, 5 April 1993  
*Resistance development in vitro and in vivo to inhibitors of HIV reverse transcriptase*
- 93.11L Sixth international conference on antiviral research, Venezia, Italy, 25-30 April 1993  
*Clinical implications of drug resistant HIV*
- 93.12L Hoechst SBU Anti-infectives - Chemotherapy, Frankfurt, Germany, 18 May 1993  
*Development of drug resistance, in vivo and in vivo, in HIV infection*
- 93.13L International AIDS Therapy Group Symposium, June 5, 1993.  
*Summary of the Second International HIV Drug Resistance Workshop, Noordwijk, the Netherlands, June 3-5*
- 93.14L Rami-93: 7th International congress on rapid methods and automation in microbiology and immunology; Human retrovirus infections, London, UK, 12-15 September 1993  
*Significance of strain variation in HIV infections during treatment*
- 93.15L 3rd Workshop on viral resistance, Gaithersburg, MD, USA, 19-22 September 1993  
*The appearance of resistance mutations in patients undergoing 3TC therapy*
- 93.16L Nevirapine Investigators Meeting, Ridgefield, USA, 9 December 1993  
*Activity and resistance with alternating regimens*
- 93.17L The First National Conference on Human Retroviruses and Related Infections, Washington DC, USA, 12-16 December 1993  
*Acquisition of 3TC resistance mutations coincides with an increase in viral load*

- 93.18L The First National Conference on Human Retroviruses and Related Infections, Washington DC, USA, 12-16 December 1993  
*Viral phenotype: why bother?*
- 93.19L Center for AIDS Research at Stanford, University of California , 22 December 1993  
*Acquisition of 3TC resistance mutations coincides with an increase in viral load*
- 94.01L Post-graduate course Infectious Diseases, Grindelwald, Zwitserland, 29 januari-6 februari 1994  
*HIV: resistance problems*
- 94.02L Antiviral therapy: Clinical Trial to Clinical Practice, Centro Congressi Milanofiori, Milano, Italy, 17 maart 1994  
*Virological studies: implications for the treatment*
- 94.03L HIV-update: Internistendagen 1994, Veldhoven, 28 april 1994  
*Virus 'load' en virusresistentie en de consequentie voor behandeling*
- 94.04L Seminaire du Centre de Recherche Public-Sante' Luxembourg 10 may 1994  
*Virological evaluation of HIV therapy*
- 94.05L Hopital Rotchild and University Pierre et Marie Curie, Paris, France 2 june 1994  
*Resistance to antiretroviral drugs and clinical relevance*
- 94.06L Department of medical microbiology. Academic University Hospital, Utrecht. 15 june 1994  
*Antiretroviral therapie en resistentie.*
- 94.07L 4 Münchener Aids-tage 1994, München, Germany. 24 june 1994  
*Controversial Topics on antiretroviral resistance*
- 94.07L Roundtable Session: Challenges and Choices in Managing HIV Disease. Pro Health Roundtable, Washington, D.C. 7 July 1994  
*Viral Resistance: Implications for Strategy*
- 94.08L International Virology Committee Meeting, August 2, 1994, Kauai, Hawaii  
*HIV antigen and HIV RNA response during therapy with RT inhibitors*
- 94.09L Perspectives therapeutiques au stade precoce de l'infection par le HIV; 37e Journée de l'Hôpital Claude-Bernard, vendredi 23 september 1994.  
*Faut-il traiter les asymptomatiques à taux de lymphocytes CD4 'subnormaux'? Table Ronde.*
- 94.10L Surrogate Markers of HIV: Strategies and Issues for Selection and Use. October 12-14, 1994, Alexandria, Virginia; member of the scientific advisory committee for workshop IV session  
*Relationship between drug resistance development and viral load*
- 94.11L First International Meeting about HIV-CMV. November 10-11, 1994, Barcelona, Spain.  
*Clinical significance and use for the therapeutical treatment of fenotypical studies in HIV patients.*
- 94.12L First meeting of informal working group on prevention of mother-to-infant transmission of HIV. December 5, WHO, Geneva Switzerland.

- 95.05L Deutscher Kongreß für Infektions- und Tropenmedizin. Berlin, 15.-18. März 1995.
- 95.06L Clinical Consensus Regional Meetings World Health, 18-21 May, 1995, New York, USA
- 95.07L Consensus Symposium on Combined Antiviral Therapy, July 25-27, 1995, Lisbon, Portugal  
Member of the Consensus Panel *Sequential Use of Combinations*
- 95.09L Medische informatie-avond HIV Vereniging Nederland, Amsterdam, 5 september 1995  
*Herinfectie*
- 95.09L Dägna (German Association of Physicians in Private Practice treating HIV-Infected Persons) Workshop, Cologne, 9 September 1995  
*New diagnostic marker - esp. Virus Load*
- 95.09L UIFI Seminar, 12 september 1995, Academisch Ziekenhuis Utrecht.  
*Repliatie van resistente HIV varianten in vitro en in vivo*
- 95.09L Antiretroviral Resistance Symposium, September 20, 1995, San Francisco, USA  
*Antiretroviral Drug Resistance*
- 95.10L Comprehensive Management of HIV Disease: VI Annual HIV Speakers Forum Meeting, October 6-7, Amelia Island, Florida, USA.  
*Treatment from a Virologist's Perspective*
- 95.10L Vergadering Levercluster EUR, Academisch Ziekenhuis Dijkzigt, 13 oktober 1995, Rotterdam  
*Antiviral Therapy & Drug Resistance*
- 95.10L Symposium on Surrogate Markers of HIV: Strategies and Issues for Selection and Use. 16-18 October, McLean, Virginia, USA  
*Chairman, International Clinical Trial Groups Subcommittee*
- 95.10L IVE Congres du Groupe de Virologie Medicale: Charge virale et nouvelles approches en virologie moleculaire, 27 Octobre, 1995, Toulouse, France  
*Antiretroviral resistance*
- 95.11L Symposium "10 jaar AIDS zorg in het Academisch Ziekenhuis Nijmegen", Nijmegen  
*Dynamiek van de HIV-infectie: consequenties voor therapie*
- 96.01L Workshop on Virological Markers in HIV Infection, Rome, Italy  
*Viral Resistance*
- 96.01L Expert's Roundtable on Retroviral Therapy, Washington DC  
*Preclinical Aspects of Resistance to Protease Inhibitors*
- 96.01L The Third Conference on Retroviruses and Opportunistic Infections, Washington DC  
*Antiviral Therapy: Viral Dynamics and Resistance; A Change in M184V Delays Development of Zidovudine Resistance in Patients Receiving 3TC*
- 96.02L Workshop Virologie, SmithKline Beecham, 1-4 februari, Harlow, Engeland  
*Antivirale therapie bij herpes en hepatitis infecties.*



- 96.04L Bristol-Myers Squibb Symposium "Antiretrovirale Therapie", April 14, 1996, Wiesbaden, Germany  
*Emerging Resistance in Antiretroviral Therapy.*
- 96.04L Spanish Meeting on AIDS, 17 april, Santiago de Compostela, Spanje.  
*Drug resistance to protease inhibitors.*
- 96.04L Academisch Ziekenhuis Groningen Refereeravond Interne Kliniek, 18 april, Groningen  
*Ontwikkeling van drug-resistente HIV varianten: in vitro en in de patiënten.*
- 96.04L Bristol-Myers Squibb Antiviral Advisory Board Meeting, April 20 - 21, Vienna, Austria  
*Viral resistance: fidelity vs. host/parasite interaction.*
- 96.07L XI International Conference on AIDS, July 7 - 12, Vancouver, Canada:  
F. Hoffmann-La Roche Ltd Satellite Symposium, July 7  
*Proteinase Inhibitors*
- 96.07L Symposium Viral Load: Impact in the evaluation of HIV therapies, July 11  
*Viral load - lessons learned from Delta, and their application to patient management*  
Speaker at the plenary session (201 and 236)
- 96.07L Roche Products Ltd. Taipei, Taiwan. AIDS Conference 27-28 July, 1996  
*Update on HIV treatment today and the role of new treatment options*
- 96.09L Symposium "AIDS, de stand van zaken", AZU Interne Geneeskunde  
*Virusbelasting*
- 96.09L II International Consensus Symposium on Combined Antiviral Therapy and Implications for Future Therapies. September 8 - 10, 1996, The Hotel Husa Palace, Barcelona, Spain.  
Co-Chair  
Session IV: Clinical Evaluation of Combination Therapy: HIV. AZT & DDC - AZT & DDI, *Delta Study - Virology*  
Presentation abstract Rob Schuurman: *The observed increase in enzyme fidelity of the 184VAL variant is not sufficient to prevent the generation of double resistant HIV-1 viruses in vitro and in vivo.*
- 96.09L Bristol-Myers Squibb, 3 September 1996, Woerden  
*Virus Load*
- 96.09L CHI, "Advances in Nucleic Acid Amplification & Detection" Conference, 18 - 19 September, 1996, Okura Hotel, Amsterdam, the Netherlands.  
*Molecular Quantification and Characterization of Drug-Resistant HIV.*  
Session's Chair
- 96.10L BHK Communications Ltd. New Drug Developmen in HIV Disease: advances in treatment strategies, 12-13 October, 1996, London, United Kingdom.  
*Exploiting the potential for reverse transcriptase inhibition. Non-nucleotide reverse transcriptase inhibitors.*
- 96.11L Roche Advisory Board Meetings on HIV and CMV, 1-2 November, Birmingham, UK.
- 96.11L Third International Congress on Drug Therapy in HIV Infection, 3-7 November, Birmingham, United Kingdom.  
*Member of the Scientific Committee*

*Chair Scientific Programme "Antiviral Resistance (virological and immunological monitoring).*

- 96.11L Roche Satellite Symposium "HIV Therapy - Perspectives in Profile", 14 November  
Sydney, Australia.  
*"Resistance and Cross Resistance - implications for treatment"*
- 96.11L Roche Panhellenic Congress, 14-17 November, Athens, Greece.
- 96.12L Bristol-Myers Squibb Antiviral Advisory Board Meeting, 5-7 December, New York
- 97.01L Roche Invirase Investigators Meeting, 21 January, Arlington VA, USA  
*Preliminary Virology Data - NV15107*
- 97.01L Minisymposium "AIDS-zorg in de praktijk", 31 januari 1997, Slot Zeist te Zeist.  
*Virologie*
- 97.02L Third International Symposium on "Treatment of HIV and CMV infection," February  
22, Barcelona, Spain.  
*Resistencia a los inhibidores de la proteasa. Bases para tomar decisiones  
terapeuticas.*
- 97.02L Conducting Clinical Trials in HIV Disease Therapy - problems, pitfalls, potential.  
February 24 - 26 February, London.  
*Resistance to antiretroviral drugs. Resistance Interactions.*
- 97.03L The 10th SB Kurhaus Workshop on Infectious Diseases, March 13 - 14, Kurhaus  
Hotel, Scheveningen.  
*New strategies in antiviral drug design.*
- 97.03L Management of HIV, CMV and Hepatitis Infections, March 14 - 16, New York, USA.  
*Positioning of drugs in relationship to the development of cross-resistance.*
- 97.03L HIV Population Dynamics, Variation and Drug Resistance Workshop, March 17 - 19,  
Edinburgh, Scotland.  
Session Chairman  
*Evolution of 3TC resistant viruses in vitro and in vivo, role of fitness and fidelity.*
- 97.04L Voorjaarsvergadering van de Nederlandse Vereniging voor Medische Microbiologie  
en de Nederlandse Vereniging voor Microbiologie, Lunteren, 22 - 23 April.  
*Virologische evaluatie van antiretrovirale therapie.*
- 97.04L Bristol Myers - Squibb Seminar: The biological bases of AIDS: clinical studies, 24-26  
April, Segovia, Spain.  
*Resistance to anti-HIV drugs.*
- 97.05L 13th British Scandinavian Conference on Infectious Diseases, in collaboration with  
the infectious diseases society of the Netherlands and Flanders, Gent, Belgium, May  
1-3.  
*HIV antiretroviral resistance.*
- 97.05L Department du SIDA et des Retrovirus, Institut Pasteur, Paris, France, May 23.  
*Replication of drug-resistant HIV in vivo and in vitro.*
- 97.05L Expertmeeting Herbesmetting, SAD-Schorerestichting, Amsterdam, 29 mei.  
*Virologische theorieën en bewijzen van hiv-her/superinfectie.*

- 97.06L Murex 1997 Users Meeting, Macclesfield, UK, June 19 - 20.  
*The principles of HIV Drug Resistance.*
- 98.02L International Symposium on Viracept (nelfinavir), Sevilla, February 28, 1998.  
State of the art lecture *Resistance and cross-resistance with protease inhibitors.*
- 98.03L II Convegno Nazionale A.I.D.S. e Donna, Napels, March 26-28 1998.  
*Profili sulla resistenza ai farmaci antiretrovirali nei diversi comparti-menti.*
- 98.04L Murex Ontbijtsymposium "Information for Life" , Wetenschappelijke Voorjaarsvergadering NVMM/NVvM 1998, Veldhoven, April 21-22, 1998.  
*Toekomst van HIV-resistentiemetingen voor de klinische praktijk*
- 98.04L Refereeravond AZL, Leiden, April 29, 1998  
*Effecten van HIV-replicatie en HIV-therapie*
- 98.06L Cursus Klinische Hepatologie van de Nederlandse Vereniging voor Hepatologie, 3-5 juni 1998, Academisch Ziekenhuis Utrecht.  
*Dynamiek van hepatitis C virus, lering van HIV.*
- 98.10L Microsymposium Opportunisme in de infectieziekten, 47ste Wetenschappelijke Vergadering VIZ, Utrecht, October 16, 1998.  
*Diagnostiek en consequentie van resistentie bij non-HIV virus.*
- 98.10L 47ste Wetenschappelijke Vergadering VIZ, Symposium "Opportunisme in de infectieziekten", Utrecht, October 16, 1998.  
*Diagnostiek en consequentie van resistentie bij non-HIV virus.*
- 98.10L ATP DR Fax Symposium: Resistance assays in clinical practice, St Thomas' Hospital, London, UK, October 22 1998.  
*Search for Solutions.*
- 98.11L Clinical Implications of HIV Drug Resistance Monitoring, 9-10 December 1998, Washington DC, USA. Session: "Focus on methods to monitor HIV drug resistance".  
*Phenotypic resistance assays.*
- 99.01L Stanford University School of Medicine, Center For AIDS Research, Stanford, California, USA, January 8, 1999.  
*New directions in resistance testing.*
- 99.03L Resistance Think Tank Meeting, Four Seasons Hotel, New York, USA, March 19, 1999.  
Session: Clinical Strategies for Dealing with Resistance  
*The Future of Clinical Use of Resistance Testing*
- 99.03 6th Annual International Discussion on HIV Dynamics and Evolution, CDC, Atlanta, Georgia, US, March 26-29, 1999.  
Session: Dynamics and evolution of HIV antiviral resistance.  
*Evolution and modeling of Zidovudine Resistance.*
- 99.04L V National Congress on AIDS; Satellite Symposium "Detection of transforming the therapeutic strategy. Towards an individualized therapy transforming the therapeutic strategy", Congress Palace, Santiago de Compestela, Spain, April 13-16, 1999.  
*Therapeutic strategies with the use of genotypic resistance methods. New and*

*experienced patients.*

- 99.04L NIV, 11<sup>e</sup> Internistendagen, Kongrescentrum Koningshof, Veldhoven, The Netherlands, April 22, 23, 1999. Parallel Session, Nieuwe therapeutische mogelijkheden voor virusinfecties.  
*Virale resistentie: klinisch belang?*
- 99.04L 4<sup>o</sup> Encuentro en Segovia, Virología; Vanguardia Científica y Práctica Clínica, Segovia, Spain, 23-24 April, 1999. Mesa 3 Future trends in the management of HIV infected patients.  
*Fitness of drug resistant HIV in vitro and in vivo.*
- 99.05L F. Hoffmann-La Roche Fortovase Launch Meeting, Geneva, Switzerland, May 8, 1999.  
*The GREAT study. Rationale for GREAT study (evidence-based decisions) plus trial details; to include DSS algorithm.*
- 99.06L Roche Diagnostics Workshop at WorldLab '99, Florence, Italy, 9-10 June 1999. Workshop 5 "Tailoring diagnostics and treatment to create integrated healthcare solutions".  
*Use of genotype testing to improve HIV therapy.*
- 99.06L Xth Symposium on HIV Infection, Visible Genetics Symposium, Toulon, France, June 17, 1999. "Standardization of HIV Drug Resistance Testing in Routine Clinical Practice".  
*Introduction*  
*The European VIGILANCE Surveillance Program*
- 99.09L 9. Deutscher Workshop der DGNÄ, Fortbildung für Ärzte und kooperierende Berufsgruppen zur HIV/AIDS-Problematik, Köln, Germany, September 4, 1999.  
*Resistenzen*
- 99.09L Training program on new trends in Diagnostic & Treatment of HIV, Roche, Montreal, Canada, September 10-12, 1999.  
*Resistance -Genotyping & Phenotyping*  
*Update on CHEESE study*
- 99.10L IIInd Workshop of European Paediatric HCV Network (APHN), Turin, Italy, 4-5 October 1999. *Virologic aspects involved in the vertical transmission of HCV and disease progression: facts and speculations*
- 99.10L British HIV Association Autumn Meeting 'HIV Treatment Guidelines', Royal College of Physicians, London, United Kingdom, October 9, 1999.  
*How to change therapy based on resistance*
- 99.10L Programma Feedback Meeting, Utrecht, The Netherlands, 12 oktober 1999.  
*De klinische betekenis van resistentie*
- 00.04L V Reunion Nacional sobre el SIDA, Pamplona, Spain, April 6th 2000.  
*HIV drug resistance. State of the art.*
- 01.02L Nascholingscursus Infectieziekten, 8-10 februari 2001 te Noordwijkerhout.  
*HIV resistentie.*
- 01.05L 4<sup>o</sup> Abbott voorjaarsbijeenkomst, Middelburg, The Netherlands, 12 april 2001.

*Resistentie in vitro.*

- 01.09L Symposium bij de aanbieding aan de Minister van Volksgezondheid, Welzijn en Sport, mw. Dr. E. Borst-Eilers, van het eindrapport van het ATHENA project. *Behandeling van HIV in Nederland: resultaten van drie jaar monitoring van geïnfecteerde patiënten na de introductie van HAART.* 12 september 2001.
- 01.11L 3rd International Workshop on HIV Eradiction, Spain 16 November 2001. *Complete inhibition of viral replication, can we achieve it?*
- 02.02L Virology: A New Perspective Conference, Victoria Australia, 14-17 februari 2002. *How to interpret HIV drug resistance?*
- 02.09L HIV-Resistenz-Workshop Viruslast, CD<sub>4</sub>-Zahl und Resistenz-Scheideweg zum Therapieoptimum. Berlin, 20 september 2002. *Update on Protease Inhibitor Resistance.*
- 02.10L Course in HIV resistance and pharmacology - From laboratory to patient. Stanford University, 1 en 2 oktober 2002. *When and How to Use Resistance Tests.*
- 02.10L Bijeenkomst nascholing apothekers. Amsterdam, 30 oktober 2002. *Klinische toepassingen van HIV resistentie bepalingen.*
- 02.11L Controversies and complementarity, or what do we (really) learn from our neighbours? A joint meeting of the: Société Belge d'Infectiologie et de Microbiologie Clinique / Belgische Vereniging voor Infectiologie en Klinische Microbiologie (SBIMC/BVIKM; 19<sup>th</sup> meeting); Vereniging voor Infectieziekten (VIZ), and Nederlandse Vereniging voor Medische Microbiologie (NVMM). Antwerpen, 7 en 8 November 2002. *HIV genotyping: yes or no?*
- 02.11L Zesde Nationaal Congres SOA - HIV - AIDS. Amsterdam, 29 november 2002. *Debat: Mag risico op resistentieontwikkeling een reden zijn om geen grootschalige behandelprogramma's in ontwikkelingslanden op te zetten?* Georganiseerd door de Artsen zonder Grenzen.
- 03.03L Refereeravond Maatschap Artsen-Microbioloog Brabant. Tilburg, 12 maart 2003. *HIV-genotypering.*
- 03.04L Education Course for Medical Doctors (University Milano / University of Utrecht April 13-16, 2003.). *HIV and antiviral-drug resistance.* Lecture date: April 15<sup>th</sup> 2003.
- 03.09L Short Course on ARV Therapy (SCART), Antwerp, 1-19 September 2003. *Resistance: genotype/phenotype.* Lecture date: September 10<sup>th</sup> 2003.
- 03.09L De toekomst van onderzoek in en over Afrika aan de Universiteit Utrecht. *HIV resistentie in de derde wereld.* Dinsdag 30 september 2003.
- 03.11L The 4rd International Workshop on HIV Eradiction (Barcelona). *Complete and continuous viral inhibition, where do we stand?* Lecture date: November 14<sup>th</sup> 2003. Charles Boucher co-chaired this meeting.
- 03.11L Hoffman La-Roche's Physicians Forum Meeting. Workshop 4: *Optimizing the opportunity - individualizing background therapy.* Together with Jonathan Schapiro, Dan Kurizkes and Deenan Pillay. Lecture date: November 16<sup>th</sup> 2003.

- 03.12L Zevende Nationaal congres SOA \* HIV \* AIDS. Workshop HIV en AIDS. *HIV-resistentie: hoe ernstig is het?* Suzanne Jurniaans (AMC, Amsterdam). Referent: Charles Boucher. Maandag 1 december 2003
- 03.12L Therapeutic Drug Monitoring van anti-HIV middelen: toepassingen en beperkingen. Minisymposium ter gelegenheid van de promotie van drs. R.E. Aarnoutse. *Het IQ concept; farmacologie ontmoet virology*. Dinsdag 2 december 2003
- 03.12L *Resistentie Problematiek*, presentatie gehouden op 14 december 2003 tijdens de 1e HIV/AIDS Workshop/nascholing voor Nederlandse HIV behandelaren (11 tot en met 18 december 2003, Paramaribo, Suriname).
- 04.02L Fuzeon Update (Roche Nederland B.V.): Workshops '*FUZEON, leren van elkaar*', gehouden op 19 februari 2004
- 04.03L Paul Ehrlich, Combating Pathogens and Cancer, Symposium to Mark the 150th Anniversary of Paul Ehrlich's Birth. Presentatie gehouden op 16 maart 2004 *Development of HIV Resistance: Clinical Implications and Fitness Costs*.
- 04.04L *Triple nucleoside regimens and drug resistance*, presentation held on April 2nd 2004 during the 5th International Workshop on Clinical Pharmacology of HIV Therapy in Rome.